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"I would have everie man write what he knowes and no more."—MONTAIGNE

BRITISH JOURNAL OF ANAESTHESIA

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EDITORIAL

SAFE WORKING SPACE

No patient would like to feel that those who safeguard lives during surgical operations should have to work at a disadvantage through lack of space or for any other reason. Small anaesthetic rooms cause difficulties for the anaesthetist, and patients can be made aware of all those preparations which, though comparatively trivial, are likely to stimulate unfortunate ideas in nervous people.

The Ministry of Health publication, *Hospital Building Bulletin No. 1 (Operating Theatre Suites)*, 1957, reprinted in 1959, differentiates between anaesthetic rooms in teaching and non-teaching hospitals. An area of 150–165 square feet is considered adequate for the latter. Hospital architects tend to keep within the limits imposed in this manual, but so far very little new building has taken place; when it does, as it surely will, anaesthetists may find that there is less space in the new hospitals! A few considerations will show how 165 square feet is not enough.

An operating table, or a patient's trolley, measures roughly 6 feet by 2 feet, and the space occupied by one man standing is approximately 2 square feet (see fig. 1). An anaesthetic machine occupies roughly 2 square feet, and a reasonably sized wall cupboard would project 2 feet into the room. Fixed furniture in the form of cupboards, a sink and draining board can be conveniently placed along one wall. A person standing beside a patient on an operating table would normally be separated from it by about 1 foot. A nurse usually stands to one side of the table, and a further 2 feet clearance should be allowed for another person to pass between her and the wall or a cupboard.

If the patient moves into the theatre feet first, and the doors from the anaesthetic room open into the theatre, it will be necessary to allow for 3 feet between the foot of the table and the doors. The anaesthetist stands at the head end of the table and the anaesthetic machine is placed about 1 foot away and a little behind him as a rule. The doors from the main corridor open inwards, and if each is $2\frac{1}{2}$ feet there should be at least 3 feet between the anaesthetic machine and the edge of the closed door. These dimensions, 14 feet by 16 feet (224 square feet), will allow an assistant to walk round the room during the induction of anaesthesia, but only with the doors closed. Teaching hospitals would require more space to accommodate students and to allow for the operation of research equipment.

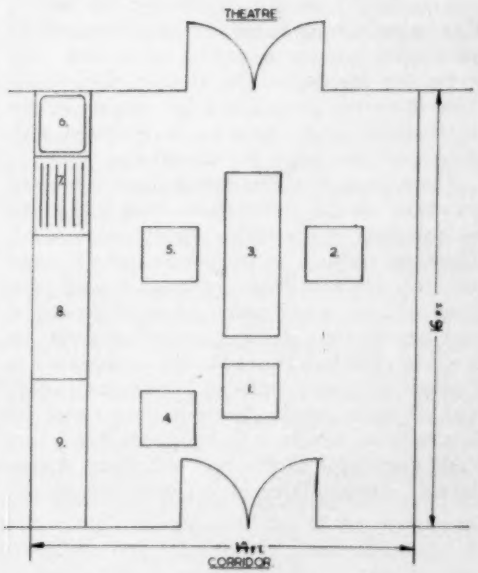

FIG. 1

Equipment in an anaesthetic room of 224 square feet

1. Anaesthetist
2. Nurse
3. Patient's trolley
4. Anaesthetic trolley
5. Instrument trolley
6. Sink
7. Drainer
8. Workshop
9. High level cupboard

Why should the anaesthetists of this country have to get used to opening doors crashing upon either the foot of the table or the anaesthetic machine, or to receive a jolt from a person passing by at the critical moment when a needle is being inserted into a vein? When a patient has to be placed into the modified Lloyd-Davis position for an abdomino-perineal operation the provision of only 165 square feet will severely restrict activity. An area of some 224 square feet is a bare minimum but is considered more than enough by the Ministry of Health!

BOOK REVIEW

Fortschritte der Kiefer- und Gesichts-Chirurgie. Edited by Professor Dr. K. Schuchardt, Hamburg. Published by Georg Thieme Verlag, Stuttgart. Pp. 369; 182 illustrations. Price DM.118.

This is not a book in the ordinary sense of the word. It is a series of papers. They were read at the 8th Meeting of the German Society for those interested in face and jaw surgery. Two-thirds of the work, however, is concerned with therapeutic pain relief and anaesthesia.

The organizers of this meeting are to be congratulated on the thoroughness with which the various parts of the subject have been covered. There are sections on physiology, on the pharmacology of both local and general anaesthetic drugs, and on almost every aspect of the use of such agents. Even gas and oxygen analgesia has a special mention. Premedication is discussed in a section of its own. Induced hypotension is dealt with at some length. Space is even found for hypothermia, which, it is admitted, has a very slight application in this field of surgery. Appropriately enough, three papers deal with various approaches to the treatment of trigeminal neuralgia.

The last third of the book is concerned with the surgical treatment of hare lip and cleft palate and of fractures of the jaw, and on this the reviewer is not competent to express an opinion. The section on anaesthesia, however, presents an exhaustive picture of the present pattern of pain relief as practised in North-West Germany. The methods employed are obviously not all in line with the views of British anaesthetists, but it would serve no useful purpose to pick out the points of divergence.

It is most heartening to learn from the material published in this book that anaesthesia in Germany has advanced so far in the few years in which is has existed as a specialty in its own right. This book can be heartily commended to all those whose work deals with cases of this kind. The only proviso is that it is necessary to be able to read the German text in the original language, for although summaries in English, French and Spanish are provided these are in many instances too brief to allow the serious reader to obtain much useful information.

A. R. Hunter

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CIRCULATORY AND RESPIRATORY PHYSIOLOGY OF INFANCY AND CHILDHOOD

BY

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INTRODUCTION

IT has taken many years for the notion to find general acceptance that children are not just "small adults", but that their bodily functions differ from those of adults also in many qualitative respects.

No aspect of the child's physiology is more important in anaesthetic practice than that concerned with respiration and circulation. There are several reasons for this emphasis. First, these two systems are most profoundly affected, even under the most favourable circumstances, by surgical operation and anaesthesia. Throughout, it is to the manifestations of circulatory and respiratory functions that the anaesthetist's observations and measurements are directed. Secondly, these two systems—within a very brief span of time—change profoundly in the newborn and during early infancy. Thirdly, relatively minor changes in the circulation (e.g. haemorrhage) or in respiration (e.g. obstruction of the airway or the application of artificial ventilation) may have far more serious effects in an infant and small child than the experience with an older age group would lead one to expect.

The profound haemodynamic changes that accompany the anatomical transformations from the foetal to the neonatal circulation are well known, although many details remain to be clarified. The end of intra-uterine existence requires complex adjustments in the neonatal body, most marked (because they are of immediate consequence) among respiratory and cardiovascular functions. There then follows the period of less striking, but no less significant, changes until the establishment of an adult-type pattern of control and regulation.

Three phases may conveniently be differentiated in this development from a neonatal to a mature respiratory and circulatory system. The first, which is one of rapid transmutation, concerns the commencement of spontaneous respiration and is associated with a number of circulatory alterations which result, in part at least, from the expansion of the lungs. This phase is as short as the changes within it are profound. It is of necessity followed by a phase of consolidation, in which the internal control of respiration and the readjustments within the circulatory system are stabilized. Some parts of this consolidation may be delayed for hours or days—rarely even weeks (e.g. closing of a patent ductus arteriosus).

The next phase, reached by easy transition from the neonatal one, is marked by a gradual adoption of the childhood pattern of circulatory and respiratory regulation.

Once early childhood is reached (2–3 years of age), subsequent changes are qualitatively insignificant and quantitatively very gradual. The only "break" in a seemingly smooth transition to a fully adult pattern occurs during puberty, which in some children is characterized by a highly labile circulatory system, until the various humoral and nervous factors which may affect it have become stabilized.

One difficulty in elucidating and expressing the differences and similarities of the child in comparison with the adult lies in the absence of a reliable and consistently valid standard of reference. Should respiratory and circulatory data obtained in a child be presented in terms of weight, height, surface area or metabolic rate? Each of these may be open to serious objection and, where calculation by weight may exaggerate one parameter of the child's performance in relation to adult values, reference to metabolic

rate may do the obverse. Many of the child's bodily functions are most rationally considered in terms of both an absolute and a relative standard.

As a general rule, values obtained in the infant are perhaps best related to metabolic rate or surface area, while in the older child the more usual reference to a unit of weight will allow a reasonably accurate comparison with adult values similarly expressed. The surface area (in square metres) of children can be obtained from their height and weight by means of the nomogram constructed by Talbot et al. (1952).

Metabolic rate (cal/hour/square metre body surface) reaches a peak in infancy, when it is about 60 cal; a second peak is recorded any time between beginning school-age and adolescence (about 40 cal), until adult levels of 30–35 cal are reached.

Oxygen consumption of the newborn (which after all is the basic need to be met by the cardiorespiratory system) has recently been found by Cross et al. (1957) to be about 6 ml/kg body weight/min, a value which is similar to that obtainable from Benedict and Talbot's tables (1921) and is about one and a half times the adult average (3.5–4.0 ml/kg/min). Once the neonatal stage is passed, oxygen consumption (ml/min/kg body weight) gradually falls to adult levels.

(A) RESPIRATION

Technical difficulties have prevented more than sporadic measurements of most respiratory functions in the newborn and young child. None the less, certain facts emerge.

I. Initiation of breathing.

The question of the baby's "first breath" has attracted much attention, because the expansion of the lung in the newborn is of primary importance, not only in the establishment of an independent respiration but also in the transformation of the circulation from its foetal course. However, there has been little agreement about the responsible factors (Smith, 1959). The role of hypercapnia and hypoxia—acting directly on the medullary centres or indirectly, via the chemoreceptors, in the initiation of spontaneous respiration—remains uncertain.

The "visible" respiratory pattern of the newborn, once spontaneous respiratory movements have been established, varies widely between individuals, and even from minute to minute for one individual. The two extremes are (1) the responsive infant who inhales and exhales rhythmically at once on delivery and (2) the often totally unresponsive infant who has long periods of apnoea, interrupted by irregular gasps. Smith (1959) states that the one is generally the product of a normal delivery, with little or no anaesthesia of the mother, while the other will have emerged only after a long and difficult delivery, during which the mother has usually received large amounts of sedatives and anaesthetics. Experimental work (Graham, 1959) makes it seem possible that marked hypercapnia (the consequence of prolonged neonatal apnoea or hypopnoea) may activate the still hypothetical "gasping centre"; whose existence was postulated many years ago (Lumsden, 1923).

In any case, blood carbon dioxide tension has been found to vary widely in the normally breathing newborn, but it would seem that the respiratory centre of the newborn (once normal respiration is established) adjusts respiration to achieve a lower carbon dioxide tension than is normally found in children and adults.

II. Response to oxygen and carbon dioxide.

Once breathing is established, carbon dioxide in concentrations as low as 0.5 per cent in the inspired air will stimulate respiration. However, the stimulating effects of carbon dioxide in the newborn depends on the percentage of oxygen in the inspired mixture, since it is greater at high (95 per cent) than low (12 per cent) concentrations of oxygen.

On the other hand, Cross and Warner (1951) found that infants aged 2 to 7 days responded to the inhalation of 15 per cent oxygen with an immediate increase in respiratory rate and minute volume, while the opposite result was obtained by the inhalation of 100 per cent oxygen.

Some of these effects are presumably due to chemoreceptor activity, and it is worthy of note (and of some practical importance) that animal experiments—and inference from human data—suggest that the chemoreceptors have a higher threshold to stimulation just before and immediately after full-term delivery: drugs which stimulate respiration via their action on the chemoreceptors are less potent at these times.

III. Effects of hypoxia.

Resistance to the harmful effects of hypoxia gradually declines from the foetal to the neonatal stage. Arterial oxygen levels of as low as 77 per cent produce no signs or symptoms in the newborn (Graham et al., 1950). A curious finding in this connection is the lowering of the metabolic rate (by as much as 50 per cent) of the newborn on exposure to an atmosphere low in oxygen (10–15 per cent). This response has recently been shown in animals to be dependent on environmental temperature (Hill, 1959). At the environmental temperature at which the metabolic rate is basal ("neutral" temperature in human newborn infants is about 34–35°C), oxygen consumption is not affected by reducing the oxygen concentration of the inspired air to as low as 10 per cent. On the other hand, if the environmental temperature is below the "neutral" temperature, oxygen consumption falls markedly; rectal temperature falls pari passu.

Periodic breathing is a frequent pattern during the newborn period, especially among premature infants. Such children have been found to have normal or almost normal oxygen saturation of the arterial blood: but on inhalation of high concentrations of oxygen the periodicity usually disappears, respiratory rate is increased, and pulmonary ventilation improved (Graham et al., 1950). Cross (1954) has suggested that a "purpose" of periodic breathing is to help the lungs expand fully through the unusually deep breaths which are part of this pattern.

IV. Physical state of the lung.

The first breath of the newborn has been estimated (Wilson and Farber, 1933) to require a pressure of 15–25 cm of water in order to separate the epithelial surfaces of the unfilled alveoli and bronchioles and expand the lungs against the "pull" of the elastic and smooth muscle tissue of the lung parenchyma. Once expansion has been achieved, inspiration requires only 5–15 cm of water to overcome the elastic and smooth muscle resistance and the flow-resistance of air in the narrow air passages of the infant (the last factor is to lose much of its quantitative importance with the growth of the lung). The high flow resistance in the small air passages of the infant's lung will be further reduced by the presence of secretions. It has also been suggested that the establishment of the pulmonary circulation, by causing capillary "erection", aids in the expansion of the lungs at birth.

The pressure required of the infant for initial expansion is well within the range of maximal negativity which premature and other newborn infants have been shown to be able to exert, i.e., about 40–50 cm of water (Cooke et al., 1957). The amount of air inhaled by the infant for each cm of water pressure ("compliance") is, on a weight-and-size basis, about half to one-third that of an adult; expressed in relation to functional residual capacity it is similar (Cook et al., 1957). Compliance probably rapidly increases during the first few minutes after the onset of spontaneous respiration at birth.

V. Lung volumes and functions (table I).

(1) *Respiratory rate.* This varies widely, even within one age group. In the neonatal period it is not dependent on weight, age or maturity. Although an average of 40 breaths per min has been calculated, the normal range from 20 to 50 makes such an average figure of little practical value. Taking a large number of readings in many children at different ages, a general downward trend—marked in the first few months of life, more gradual until school age—is, however, evident. Extremes of rate or, more important, marked changes within a short period of time, are significant signs of respiratory distress and thus of potential respiratory failure.

The body usually functions at the most economical level possible. Thus normal breathing is "set" at a level which involves the minimal expenditure of energy. The work of breathing (as performed by the muscles of respiration) is altered, for a given alveolar ventilation, in accordance with changes in rate and tidal volume. The high respiratory rate of the infant is apparently the one at which minimal work is expended. The anatomy of the newborn thorax is a factor in this. Inspiration is largely accomplished by diaphragmatic movement, which is limited, no matter what the muscular force. Additional inspiratory volume through an increase in the transverse and antero-posterior diameter of the thorax can be achieved only at a later age, when growth of the thorax and an oblique position of the ribs, allow expansion of the rib cage as a whole.

TABLE I

Normal values for lung functions for persons of various sizes.

Age	1 wk.	1 yr.	3 yr.	5 yr.	8 yr.	12 yr.	15 yr.	♂ 21yr.	♀ 21 yr.
Height (cm)	48	75	96	109	130	150	170	174	162
Weight (lb.)	6.5	22	32	40	58	85	125	160	125
FRC (ml)	75*	(263)	(532)	765	1200	1750	2500	3200	2900
VC (ml)	141†	(475)	(910)	1280	1900	2800	4200	4750	4500
$\dot{V}_E$ (ml)	550	(1775)	(2460)	(2600)	(3240)	(4150)	5030	6000	5030
V_T (ml)	17	(78)	(112)	(130)	(180)	(260)	360	500	420
f (frequency)	30	(24)	(22)	(20)	(18)	16	14	12	12
$\dot{V}_A$ (ml)	385	(1245)	(1760)	(1800)	(2195)	(2790)	3070	4140	3530
V_D (ml)	6	22	32	40	58	85	140	160	125
C_L (ml/cm H_2O)	5	(16)	(32)	44	71	91	130	163	130
R (cm H_2O/l./sec)	29‡	(13)	(10)	8	6	5	3	2	2
DLco (ml/mm Hg/min)	0.2	(0.6)			(1.3)		(1.8)	2.3	
Cardiac output (l./min)	(0.9)	1.9	2.7	3.2	4.4	5.7	(7.0)	(7.6)	(7.2)
Lung weight (g.)	49	120	166	211	290	470	640	730	

* Supine.
† Crying vital capacity.
‡ Nose breathing.
Parenthesis = interpolated values.
FRC=functional residual capacity.
VC=vital capacity.
$\dot{V}_E$=minute volume.
V_T=tidal volume.
$\dot{V}_A$=alveolar ventilation.
V_D=deadspace.
C_L=lung compliance.
R=resistance to breathing.
DLco=diffusion capacity of lung (CO method).

(From Cook, C. D. (1959). Respiratory physiology in infants and children: in Smith, R. M., *Anaesthesia for Infants and Children*. St. Louis: Mosby)

By plotting the work of breathing against respiratory rate in infants, a curve is obtained with its trough at about 37 breaths per min. However, there is little significant increase in work within the range of 20–50 breaths. The rise in work at high rates is largely due to an increase in resistance to air flow in the relatively narrow respiratory passages of the infant; the increased velocity of air flow which is associated with a higher rate of breathing leads to turbulence and thereby an increased resistance.

(2) *Resting lung volume* (functional residual capacity—FRC). A number of factors—change in position, rise in abdominal pressure—may decrease the FRC, while asthma increases it. The importance of the FRC is that the air within this "volume" acts as a pool into which carbon dioxide and oxygen are mixed during the normal respiratory cycle.

(3) *Other lung volumes.* The various components change in a parallel manner with growth, increasing with approximately the third power of the height. In other words, the amount of change becomes ever greater with increasing height (Cook, 1959). A useful curve relating vital capacity to body height has recently been published, based on measurements in 180 normal convalescent children (Whalley, 1959).

As Engel has shown (1947), total lung volume (measured post mortem at normal ranges of inspiratory and expiratory pressures) increases some eightfold from birth to 8 years. The rate of growth during this period is, however, by no means constant, being very high during the first year, after which it slows down and parallels changes in body weight. The internal surface has an even higher rate of development (again, most marked during the first 2 years of life), but this change has proved more difficult to quantify.

The trachea, which contributes so largely to the anatomical deadspace (see later), doubles its volume in the first 2 years of life. But the size of the trachea relative to total lung volume

rapidly decreases over the first 2–3 years (Hall, 1955).

(4) *Ventilation.* Since the minute volume is the product of tidal volume and respiratory rate, the same value can be achieved by adjusting either variable. To increase the minute volume by an increase in tidal volume reduces the work involved in breathing. Furthermore, increasing the tidal volume will provide better compensation for a large respiratory deadspace than increasing the rate (see later).

The following values have been obtained for minute volume per kg of body weight, at different ages: newborn, 190 ml; gradually increasing to 220 ml at 1 year; then falling to 170 ml at 7 years; 140 ml at 11 years; 130 ml at 14 years and finally reaching the adult level of 95–100 ml (Köttgen and Bolt, 1954). As a rough approximation it can be stated that, *related to surface area*, there are no great changes in minute volume from infancy to maturity. Similarly, the ratio of minute volume to oxygen consumption remains approximately constant at 0.3 for all ages.

The neonatal tidal and minute volumes bear a direct relationship to weight (Cook et al., 1955), the increase in minute volume of the larger infants being the result chiefly of an increased tidal volume.

(5) *Deadspace and alveolar ventilation.* As the exchange of oxygen and carbon dioxide in the lungs takes place only at alveolar level, it is the volume of inspired gas entering the alveoli each minute, the alveolar ventilation, which is of fundamental importance. In ordinary circumstances alveolar ventilation is a function of respiratory rate, tidal volume and the anatomical deadspace (the air passages along which the inspired air is conducted but where no gas exchange takes place). While a person's anatomical deadspace is essentially constant, an additional component, the apparatus deadspace, is added during anaesthesia. Calculated per unit of weight, the anatomical deadspace is the same from infancy to maturity—1 ml/0.45 kg of body weight—and the ratio of deadspace to tidal volume also remains essentially constant at 0.3.

However, any absolute increase in deadspace (e.g. through apparatus deadspace) is more important the smaller the person, because the *added* volume will be proportionately much greater. Furthermore, the smaller the tidal volume, the more harmful (in terms of a decrease in alveolar ventilation) is any addition to the deadspace. A knowledge of the respiratory minute volume is as useful in routine circumstances as it may be misleading in others. For it is not the amount of air passing in and out of the lung that matters physiologically, but the amount which partakes in the gaseous exchange at alveolar level, i.e. the alveolar ventilation.

If the deadspace be doubled in an infant, the maintenance of the same alveolar ventilation would require either doubling the rate (tidal volume remaining the same), or increasing the tidal volume by one-third. Such calculations are based on the assumption that at high rates of breathing there is no diffusion from the anatomical deadspace to the alveoli. Any mad dog panting in the midday sun is living proof of the falseness of this assumption!

In the foregoing discussion "deadspace" has been used to mean anatomical deadspace. In anaesthesia (as in some other circumstances and in disease) there may, however, also be a "physiological" deadspace, brought about by the underperfusion or lack of perfusion by pulmonary blood of parts of the lung which are still properly ventilated: such areas would further impinge upon alveolar ventilation. The importance of this type of deadspace in anaesthesia has not yet been settled.

The addition of apparatus deadspace during anaesthesia in infants is complicated because the infant is limited in his compensatory capacities. Since breathing is largely diaphragmatic and tidal volume thus limited, minute volume can only be increased by a rise in respiratory rate in order to achieve the appropriate alveolar ventilation (tidal volume minus deadspace multiplied by respiratory rate). As has been pointed out, this is an inefficient way of maintaining an adequate alveolar ventilation.

These considerations should be borne in mind when making use of tables of ventilatory volumes, such as the nomogram of Radford et al. (1954), which predicts the basal tidal volume from the weight and respiratory rate. Although, once certain corrections are made to apply this to anaesthesia, such predictions have proved to be of practical value under ordinary circumstances;

they are no more than rough approximations which may be significantly at fault in an individual patient.

(B) CIRCULATION

1. BLOOD PRESSURE.

(1) *General aspects.*

Because it is easily accessible to reasonably accurate measurement, the blood pressure has taken on a central role in any discussion of cardiovascular functions. Yet, on further consideration, it becomes clear that blood pressure is of only secondary importance as far as the organs of the body are concerned. What matters is the amount of nutritive material which reaches the various organs and tissues, and therefore blood flow is of greater importance. The most direct way of ensuring an adequate supply of blood would be to regulate the flow itself. But this would necessitate the continuous measuring and monitoring of flow, a problem which Nature has found no easier than the engineer to solve. The alternative to indirect flow regulation by changing the perfusion pressure is therefore adopted. Since pressure and flow are directly related, the one will determine the other in a manner which depends on the properties of the vessel walls and the degree of resistance offered to flow. The monitoring of perfusion (blood) pressure is accomplished by means of the baroreceptors (in the carotid sinus, carotid arteries, aortic arch, and perhaps also elsewhere); the regulation of the blood pressure is achieved largely by changes in resistance (variations in vasomotor tone), reflexly influenced by the baroreceptor monitors. In this way blood flow can be maintained as a whole, and yet change regional supply acording to local needs.

Applying these general considerations to the neonatal circulation, its outstanding characteristic is "centralization": most of the blood circulates within an inner core, at the neglect of peripheral flow (i.e. the extremities), which is of little functional consequence at this stage. To express this differently, the arterial blood pressure is maintained at levels surprisingly close to those of an older child, even a young adult, by a very high peripheral resistance and a relatively high elastic resistance in the aorta and its main branches. The heartbeat is rapid, the stroke volume small, and the pulse pressure narrow. As a result there is very little latitude in the regulation of the circulation: the normally high peripheral resistance (probably more a matter of anatomical "restriction" in the total cross-sectional area of the vascular bed than the result of vasomotor constriction) allows little further increase to compensate in the only available manner for such events as haemorrhage or sudden change of position. The blood pressure is, therefore, labile and even minor changes may have exaggerated effects on total and regional blood flow.

Fortunately, this phase of "centralization" does not last long; within a few months the circulation begins to change towards the mature pattern, which will be described later.

Pulmonary circulation. In the lesser circulation the changes from the foetal to the neonatal pattern consist of the establishment of pulmonary flow (replacing the pulmonary artery-aorta shunt through the patent ductus arteriosus). Ultimately, with approximately the same amount flowing through the pulmonary arterial bed as passes through the systemic one, the pressure in the pulmonary artery is only about one-fifth of that in a systemic artery. In the immediate neonatal period, however, the pulmonary vasculature is still anatomically "restricted", with the result that the pulmonary artery pressure at birth is about three-quarters that in the aorta, even when the ductus arteriosus is no longer patent.

With the full expansion of the lungs and the changes in the pulmonary vascular structure, the pressure falls in a matter of hours to days, until it has reached the level of the older child. The corollary of this development is the adaptation by the right ventricle to the altered resistance of the pulmonary vascular tree. At first it has to propel the same amount of blood as the left ventricle against an only slightly lower vascular resistance. During this early phase the right ventricle is, therefore, structurally and functionally almost the equal to the left ventricle. Rather inaccurately this is described as "right ventricular preponderance" (e.g. in the electrocardiographic pattern of this stage), although the right ventricle is even then the less powerful of the two. But the term has become established as an expression of the prominence of right ventricular

structure and function compared with its later role.

The childhood pattern. While, as described, the circulation during about the first year of life is characterized by "centralization" (small stroke volume and cardiac output; high elasticity coefficient, but small volume of the central arterial bed; high resistance of the peripheral arterial bed), there gradually occurs a transition to the "release" pattern of maturity (large stroke volume and cardiac output; small central elasticity coefficient and peripheral vascular resistance) (Graser, 1959).

The curve of cardiac output and stroke volume falls linearly with age, while that for the elasticity coefficient of the aorta and large arteries and the peripheral vascular resistance fall exponentially, the two curves "crossing over" at 3–4 years of age, which thus marks the change-over from the infant to the adult pattern.

It is likely that the phase of centralization is associated with low activity of the buffer nerves. Later in childhood baroreceptor activity increases and vasomotor tone is less marked. This is, in turn associated with an increase in the cross-sectional area of the aorta and the arterial periphery. (Similar changes take place on the venous side; in fact, the cross-sectional area of the venae cavae gradually exceeds that of the aorta.)

At or soon after puberty the pulse pressure is often relatively wide, although the systolic level will be at approximately adult levels: this finding has been explained on the basis of an increased stroke volume and vagal tone which are frequently noted at that time.

(2) *Measurement of arterial pressure.*

While the sphygmomanometric method using Korotkov's sounds has been generally accepted in practice as a reliable and reasonably accurate method, which compares well with direct intra-arterial blood pressure determinations, it has its limitations in the newborn and infants. In particular, two difficulties have been experienced. One concerns the proper cuff size in relation to the circumference of the arm, the other the value of the "flush" method in neonates and infants in whom the palpation or auscultation method may be difficult or impossible to use. As for the former, comparison with direct pressure readings has provided the rough rule that the cuff should be at least one-third, preferably one-half, the width of the arm circumference (Köttgen and Bolt, 1954; Robinow et al., 1939). Too wide a cuff gives better results than one that is too narrow, but the degree of inaccuracy is usually not great, even when the "wrong" cuff is used. It is wise to have a selection of cuffs of different widths available whenever accuracy of determination is essential. Using a 2.5-cm cuff on 54 normal infants. Holland and Young (1956) found that palpation of the brachial artery below the inflated cuff gave reliable readings with very small scatter.

As for the "flush" method contradictory results have been obtained. While some workers have felt that this method gives practically reliable information about the systolic pressure, recent comparisons by Moss et al. (1957, 1958) with direct and auscultatory readings indicate that the flush method records *mean* rather than systolic pressure values. They also found that the cuff size mattered little when this method was used.

The average systolic blood pressure soon after birth is about 75–85 mm Hg and increases another 5–10 mm Hg within the first few weeks. There is little further rise. Diastolic pressure values average 40–50 mm Hg and increase 10–15 mm Hg. But the normal variation is so great that individual values, unless extreme, are of little consequence. Any marked change from a known level is significant.

II. BLOOD VOLUME.

According to Mollison et al. (1950) the blood volume of infants is almost exactly the same as that of adults, an average of 41.3 ml/kg of body weight of plasma volume and 84.7 ml/kg for total blood volume. Total red-cell mass and haematocrit were found to be directly related to one another. But per unit of body weight the blood volume of the newborn was slightly greater than that of adults.

III. CARDIAC OUTPUT.

Because of technical and other difficulties, there have been only scattered determinations of cardiac output in infants and children. Taking adult values (corrected for square meter of body surface) as reference, the cardiac output of the newborn should be about 500 ml/min. This

value agrees well with that obtained by means of the dye dilution method (Prec and Cassels, 1952) and by the Fick method during cardiac catheterization (Adams and Lind, 1957), although the range of values in all these studies was considerable. It is interesting to note that Grollmans formula—C.O. = 2.2 ± 0.3. l./sq.m body surface (Grollman, 1932)—would give similar results.

In comparison with the basal metabolic rate, cardiac output increases relatively more during the first half of childhood. It then levels off and increases parallel to the metabolic rate.

SUMMARY AND CONCLUSIONS

The development and characteristics of respiration and circulation from the neonatal period onward are reviewed and observations relevant to anaesthetic practice stressed.

Normal values are given for various respiratory and circulatory functions of the newborn, infant, and older child.

The relationship between anatomical and external (e.g. apparatus) deadspace is of great importance, particularly in the infant, for determining an adequate alveolar ventilation during spontaneous or assisted respiration.

The development of the circulation follows a distinctive sequence from early infancy to adolescence. The circulation is at first dominated by a pattern of "centralization", in which a relatively small stroke volume is discharged at a high heart rate into a small aorta against a high peripheral vascular resistance. This arrangement severely restricts compensatory adjustments of the body.

By gradual transition this pattern changes into the adult one, already present in all essentials during later childhood, in which a much larger stroke volume is propelled at a slower rate into a larger arterial bed against a much lower peripheral vascular resistance; this enables the circulation to adjust itself rapidly and accurately in order to maintain a constant blood pressure and regulate regional blood flow under diverse circumstances.

As the arterial blood pressure remains at about the same level throughout most of this development, from the infantile to the adolescent pattern, knowledge of the blood pressure level alone can only be of limited value in the assessment of the state of the circulation.

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Further particulars from

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ASPHYXIA NEONATORUM

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THIS is a subject which is bedevilled by ignorant tradition and irrational guesswork. Unfortunately the responsibilities of obstetricians, anaesthetists and paediatricians so closely overlap that unless there is very good team work between all three the baby's interests may suffer. Certainly research into the problems of asphyxia neonatorum, which is still woefully inadequate, is only to be found at a high level of achievement where all three classes of practitioner co-operate and pool their experience and several skills.

Too often the question has been raised, as though it were a political one, as to who is responsible for the care and resuscitation of the newborn. It is the urgent concern of whosoever is available to cope, and the emergency care of the newborn should be as much a part of the anaesthetist's work as of a paediatrician and obstetrician.

Resuscitative techniques are as controversial as ever and range from procedures which are either heroic or bizzare (depending on one's point of view) to the physicianly "dolce far niente" of those who believe that a baby's best chance in meeting the hazards of its birth is to be left strictly alone. Even an average cynic would have no difficulty in recognizing in many babies the dogged will to survive in spite of much that is done for them. The statistical evaluation of any technique is not easily come by, since there are too many variable factors to take into account, and the circumstances of asphyxia differ too widely to make comparisons reliable or even feasible, except within narrow limits.

Anaesthetists, with their increasingly profound knowledge of applied respiratory physiology, should be able to contribute more than hitherto to the problem, since the failure of the perinatal mortality rate to drop in parallel with the mortality rates of the rest of childhood reveals all too clearly that our present techniques, whether active or noninterventionist, are a long way from reducing the deaths from asphyxia neonatorum to the irreducible minimum.

If we look back in history we shall find the pendulum swinging this way and that. To William Smellie the matter was quite simple. The child was well whipped and had its nose rubbed with onions in order to make it cry. The use of clysters in the eighteenth century to inflate the intestines with tobacco smoke was recommended in the belief that this would establish peristalsis and thus assist, through co-operation of the diaphragm, the action of heart and lungs, whatever that may mean. Mouth-to-mouth insufflation as practised by the prophet Elisha in the Old Testament was at least more sensible.

Well into the nineteenth century things had taken a much more active turn when Schultze's method, which involved hanging the baby by its shoulders facing forwards between the operator's legs and then swinging it smartly at arms' length above his head, until at the end of the arc, the baby jack-knifed, doubled up in flexion, above and behind his head. Thereupon the baby was swung through the same arc down towards the floor, in the reverse direction. An eminent obstetrical colleague of mine claims to be one of the few survivors of this procedure. Buist described the manoeuvre in the *Transactions of the Edinburgh Obstetrical Society* in 1895 as follows: "Standing in a well-cleared space, in the midst of a small room, whose other denizens were withdrawn into the corners, my feet planted well apart and arms extended, I taught the neonatus to perform a series of grand circles while the meconium distributed itself in trajectories for which the room and its inmates, including the physician, formed a comprehensive recording surface."

Later innovations included the subcutaneous injection of whiskey (provided it was Irish) and tincture of belladonna. The use of hot and cold baths into which the baby was alternately plunged only died out in the early 1940s.

A common order of procedure in use before the 1939–45 war at a London teaching hospital (where the writer worked) was as follows. The head was sloped downward and the tongue drawn forward with forceps. It was believed that this would stimulate respiration. Oxygen or carbon dioxide was blown in the childs face, ethyl chloride might be sprayed on the surface of the body and presently, if it showed little interest in breathing, its gums were rubbed briskly with brandy. By now a hot bathtub was ready and it was plunged into this and alleged artificial respiration applied by treating it rather like a concertina. Mouth-to-mouth insufflation was often used with apparent success and, finally, when all else had failed and the child was unquestionably dead, intracardiac adrenaline was injected as a "coup de grace". From all this enough babies survived to encourage the practitioners of such techniques, until it became clear that if a baby had even half a chance of breathing it would most certainly take it, and the majority of recoveries could truthfully be regarded as independent of the measures employed. This led to a swing of the pendulum in the opposite direction, especially with the increasing interest that paediatricians have taken in the subject, and the intelligent recognition that the baby's failure to breathe was not because of cussedness calling for punitive measures, but because it was dangerously ill and therefore required the minimum of handling.

The treatment of choice lies somewhere between these two extremes and should be based upon a recognition of the physiology of the onset of respiration. It must not inflict further damage nor shock upon a baby already in serious jeopardy.

PERINATAL MORTALITY

Asphyxia neonatorum is simply the outward and visible sign of some serious underlying pathological process. It was Smith (1951) who poetically referred to "The Valley of the Shadow of Birth". At that time he recognized eight main classes of perinatal loss, namely, maceration, malformation, prematurity, trauma, infection, erythroblastosis, syphilis and anoxia. The full measure of the problem, however, is likely to be revealed by the nationwide Perinatal Mortality Survey instituted last year by the National Birthday Trust; the findings are not yet completed.

Perinatal mortality is defined as the sum of stillbirths and deaths within the first week of neonatal existence. It is now recognized that about two-thirds of the infants weigh less than 2,500 g. and are—by the usual standards of classification—to be regarded as cases of premature birth. The number of stillbirths compared with those of neonatal death is in the ratio of about two to one; approximately half the stillbirths, being macerated, are therefore outside the scope of this article; the other half die during or shortly after labour. In about two-thirds of all fresh stillbirths anoxia is the main, and often the only factor (Butler, 1959).

Of the causes of neonatal death, atelectasis, usually due to the pulmonary syndrome of the newborn, is one of the most important during the first week. Foetal abnormalities, incompatible with life, rank closely behind it. Irreparable damage to the central nervous system due to anoxia during labour is also another important cause of neonatal death. The incidence of infection is still regrettably high and in hospital practice the emergence of antibiotic-resistant strains of Staphylococcus has made the problem more acute than ever. Death may be due to gross immaturity, but what is encouraging is that intracranial haemorrhage and the mechanical trauma of delivery account for far less than 10 per cent of the total—a tribute to improving obstetrical techniques.

The importance of prenatal asphyxia is now fully recognized. It may so damage the vital centres that their responsiveness following delivery is wrecked beyond recall. Any interference with the placental circulation or with placental efficiency, as, for example, in pre-eclampsia and hypertensive states, produces mounting degrees of anoxia. Prolonged labour, especially with the membranes ruptured, increases the hazards of foetal anoxia with the passage of each few hours. Any accident of pregnancy or labour, or any drug or anaesthetic which precipitately lowers the maternal blood pressure,

reduces the foetal oxygenation. One of the commonest accidents results from anaesthesia inexpertly administered to the labouring woman. The inhalation of liquid vomit from an improperly emptied stomach is still distressingly common in indifferent obstetric anaesthesia and, although it is a potent cause of maternal death, it is even more serious as a cause of irreparable asphyxia in the baby either before or at its birth. It cannot too strongly be urged that the occasional anaesthetist has no place in the modern labour room and the now recognized hazards of obstetrical anaesthesia merit only the most expert attention. Added to all the more readily recognizable causes of prenatal anoxia undermining the baby's chances at birth are undoubtedly less determinable genetic factors.

THE ONSET OF RESPIRATION

This has been extensively studied; our belief is that a healthy baby aerates its lungs very rapidly indeed (Potter, 1952; Donald and Steiner, 1953). To achieve this, a baby has not only to overcome what Smith (1951) has described as the moist cohesion of the alveolar walls but must also divert an enormous blood flow through the pulmonary vascular bed. The initial gasps are thought to be provoked by the carotid sinus whose chemoreceptors are stimulated by anoxia and mounting carbon dioxide levels. Pressor stimuli, following the severance of placental circulation, also play a part. As soon as an adequate supply of oxygen has revived the respiratory centre, however, rhythmical breathing is initiated. We have found that the pressure swings within the thoracic cavity exerted by the baby's respiratory efforts to expand its lungs can be as high as 90 cm of water, of which negative pressures of 35 or even 45 cm of water represent inspiratory effort (Donald, 1957). The high positive pressure swings assist the baby in ridding its air passages of foreign material.

A baby fit enough to cry well at birth has the necessary energy to overcome its primary atelectasis. Our technique in making these measurements has involved intra-oesophageal electromanometry, and we have found that the pressures necessary to ventilate the lungs diminish progressively as they expand. A further very important physiological factor has been described concerning pulmonary haemodynamics shortly after birth. Born et al. (1954) have shown that the increased quantity of blood returning from the lungs not only raises the pressure within the left atrium, and so closes the foramen ovale, but that the pulmonary demands upon the circulation may reverse the direction of the blood flow through the ductus arteriosus, for a time, from left to right. By this means a fair proportion of blood does a double circuit through the lungs and receives a second exposure to oxygen. This helps to hasten the attainment of full oxygenation of neonatal blood until the percentage oxygen saturation exceeds 90 and so causes the functional closure of the ductus.

Subsequent attacks of neonatal asphyxia may re-open the ductus because of the falling oxygen saturation. Carter (1957) has stated that the lungs behave like erectile tissue due to the architectural arrangement of the lung capillaries It would thus appear that the patency of the alveoli is maintained as a result of the filling of the pulmonary capillaries. As a corollary to this, Jaykka (1957) in a series of experiments on human lungs has described how artificial respiration not only aerates the lung directly, as might be expected, but has the further beneficial effect of encouraging the erectile expansion of the pulmonary capillaries, thereby achieving more lasting benefit.

A subsequent attack of neonatal asphyxia, for example, what is popularly called a "blue" attack, has been shown by the angio-radiographic studies of Lind and Wegelius (1954) to put the whole process into reverse, with the restoration of the patency of both ductus arteriosus and foramen ovale. In respiratory difficulty after birth the initially high pulmonary vascular resistance persists and blood which should have gone through the lungs is consequently shunted into the aorta through the re-opened ductus. As a result there is less blood returning from the lungs to the left atrium, thus altering the pressure gradient between the two atria so that blood is again shunted from right to left through the foramen ovale, as in the foetal circulation, and cyanosis results.

The vascular resistance is due to the intensely coiled lung capillaries before they have been more or less straightened out by alveolar expansion.

In a successful initiation of respiration, there-

fore, there is not only the important matter of reviving the vital centres with oxygen but the establishment of the stable erection of the alveolar architecture, the lowering of pulmonary vascular resistance and the effective separation of the circulations of the right and left sides of the heart. Not only does pulmonary vascular resistance fall but, as has already been stated, the gaseous resistances to aeration likewise diminish.

Lung compliance can be regarded as the change in lung volume divided by the difference in intra-oesophageal pressures between instants of nil trachea air flow (Annotation, 1956). Changes in lung compliance can therefore be studied by the simultaneous recording of tidal air flow and intrathoracic pressures, as measured through the oesophagus, and this we have been at some pains to study (Donald, 1954; Donald et al., 1958). The technical difficulties of neonatal spirometry are too great to describe here, but it is quite clear how readily lung compliance improves with progressive aeration as confirmed radiologically. The fortunate baby whose breathing gets away to a flying start is soon rid of the need to maintain an exhausting degree of effort to oxygenate itself, in marked contrast to the efforts of the neonate in respiratory distress. Similar observations have been made by Karlberg et al. (1954) who reckon that such a baby may have to exert from two to five times as much effort to breathe as in the case of a normal child. It is very often this exhaustion which finally defeats the chances of survival.

Where, however, inadequate respiration is due to central depression the picture is very different. Here the respiratory efforts required to expand the lungs initially are not even made. It is important thus to distinguish between the mechanical difficulties of a blocked airway or atelectasis and depression of the vital centres due to anoxia, trauma, foetal shock, anaesthetics or drugs.

HANDICAPS TO THE INITIATION OF BREATHING

When confronted with the emergency of asphyxia neonatorum one has seldom opportunity or time to reflect on the causes of the baby's difficulties. Nevertheless treatment would often be more intelligent if these were kept in mind and it would be more generally appreciated that there are different types of asphyxia calling for different types of handling. No one routine of resuscitation is applicable in the face of such widely differing pathology.

I have already mentioned the competence of the respiratory centre. The commonest cause of its depression is antecedent anoxia for which, in some instances, the preceding management of the labour may be responsible. In traumatic deliveries intracranial pressure may be raised either by haemorrhage or by cerebral oedema, but a not insignificant contribution to central depression comes from the injudicious use of drugs and anaesthetics. The barbiturates are particular offenders in this respect. Morphine, pethidine and heroin at least have the virtue of having an antagonist in nalorphine but it has to be admitted regretfully that apart from regional, spinal and conduction methods of anaesthesia there is no anaesthetic agent of any efficacy which does not depress the baby's activity in parallel with that of the mother.

The peripheral circulation may be depressed by haemorrhage, anoxia and raised intracranial pressure. The recognition of this state of affairs demands the gentlest handling and treatment.

The degree to which the airway may be obstructed by mucus or inhaled meconium and blood is often overlooked, especially by those not trained in the anaesthetist's outlook.

Lastly, respiratory movements may be handicapped by prematurity and the lack of sheer strength necessary to aerate the lungs because of poor pulmonary compliance, which may be due either to immaturity, hyaline membrane disease or to both. The mechanical interference of a large diaphragmatic hernia is an important though less common cause of difficulty.

DIFFERENTIAL DIAGNOSIS OF RESPIRATORY EMERGENCIES AT BIRTH

First and most important is the recognition of a blocked airway requiring immediate clearance. More difficult is the infant whose lungs are full of aspirated liquor and meconium because these are less readily accessible to suction. Thirdly, the child's difficulty may be due simply to the persistence of anaesthetic effect. The deeper the anaesthetic, the greater the effect upon the child. Fortunately this is seldom fatal in the absence of other complicating factors. Likewise the recent

use of morphine and drugs of this class should be borne in mind as possible causes because of the ready availability of an antidote like nalorphine. Nalorphine, however, given where not indicated to antagonize such drugs can do nothing but harm, hence the importance of a careful and quick review of the possible causes of difficulty. Fourthly, the baby may already be suffering from a well-established intranatal pneumonia. This is likely if labour has been prolonged with the membranes ruptured. Intracranial damage may have been inflicted. Such a baby exhibits all the features of foetal shock, presently to be described, but cerebral oedema even in the absence of trauma for example, in hydrops foetalis, and as a result of diabetic pregnancy, is also encountered. Central depression may be due solely to severe intrapartum anoxia of the foetus. The need for oxygenation of the respiratory and vasomotor centres in these patients is urgent. Finally, there may be a gross foetal abnormality which is not immediately apparent, such as oesophago-tracheal fistula, cardiac abnormalities and diaphragmatic hernia. One could hardly expect infants in each of these categories to respond to the same automatic line of treatment.

CLINICAL FEATURES OF ASPHYXIA NEONATORUM

Traditionally neonatal asphyxia has been classed as livid or pallid, blue or white, but the difference in colour in the baby is the least important clinical feature. The baby showing deep cyanosis is demonstrating thereby a very adequate periphal circulation and the prognosis is correspondingly good, provided oxygen can reach its brain before it is too late. Neglect of blue asphyxia, which may often be due to an obstructed airway will soon lead on to asphyxia pallida in which the peripheral circulation is failing. Until this happens, however, the bodily tone of the child is good. The sphincters are not relaxed and rapid clearance of the pharynx and nasal airways usually suffices. The important thing to watch is the strength and rate of the heartbeat rather than the colour. A rapid and full bounding beat is a good sign.

As the condition deteriorates, however, the baby's heart rate slows. The colour turns more grey than white, although the lips take on a dirty purple colour. The child now lies flaccid with sagging jaw and vocal chords separated from each other in the paralyzed position and all reflexes are in obeyance. This at least facilitates intubation of the trachea. It would be better to describe this condition simply as foetal shock rather than as asphyxia pallida since the former term gives a far better picture of what is happening.

The heart rate can most easily be observed by watching the base of the umbilical stump. As the child's condition deteriorates the rate gets slower and slower and then becomes so weak that pulsation is no longer visible. The condition is now desperate. The first sign of any recovery is acceleration of the heart rate which occurs long before any improvement in tone or colour. Respiratory activity—if any is present—is either almost imperceptibly shallow or punctuated by a primitive type of gasp. Usually within about a quarter of an hour the changes are irreversible, although remarkable instances of recovery after as long as three-quarters of an hour in this state, very occasionally occur.

PREVENTION OF ASPHYXIA NEONATORUM

This is a challenge to the art of obstetrics. The signs of foetal distress in labour are the signs of asphyxia and to ignore them is to court disaster from anoxic damage to the baby's vital centres. Foetal distress demands foetal delivery and the sooner the better, whatever the stage of labour. Nowadays an increasing number of Caesarean sections are being undertaken for foetal distress occurring in the first stage of labour. While preparations for operation are being made any method of analgesia, such as nitrous oxide and air, which lowers the maternal percentage oxygen saturation should be stopped forthwith and the mother encouraged to breathe pure oxygen. Prystowski (1959) has suggested that even normal parturients should have oxygen administered routinely just before delivery for the sake of the one baby in twenty who might be suffering from some degree of hypoxia; but certainly there would appear to be real benefit in cases of foetal distress. Much, however, depends on the cause of the foetal asphyxia in utero. Walker (1954) found that the administration of oxygen to the mother had no effect on foetal percentage oxygen saturation where this was impaired by placental changes due to postmaturity.

The choice of anaesthetic is also a critical

matter. In all conditions likely to produce prenatal anoxia of the foetus, for example, diabetes, Holmes (1959) regards general anaesthesia as undesirable. By using spinal anaesthesia in all cases of Caesarean section in diabetic patients he has lost only two out of forty-one babies, a very creditable figure although it is felt that other factors must have been at work. The modern practice of carrying out, as far as possible, all vaginal operative deliveries under pudendal block anaesthesia has very much indeed to recommend it, as testified by the lively activity of these babies at birth, and such is now our routine practice whenever possible. The same benefits result from low spinal and extradural anaesthesia. General anaesthesia for Caesarean section is usually preferred. The old prejudices against thiopentone for induction in these patients have now been dispelled since it is recognized that concentration and elimination in the foetal blood follows that of the mother, and that there is no longer any need for haste to deliver the baby within three minutes. All are agreed that any depression is minimal and very short-lived if no more than 250 mg of thiopentone is given. The responsibility of the anaesthetist for the baby's condition at birth during Caesarean section is nowadays taken very seriously, but anoxia is still a more serious matter than the choice of anaesthetic agent.

Our first impressions of hydroxydione for the induction of anaesthesia in Caesarean section are favourable but no drug, however well chosen, is ever as important as the individual anaesthetist's skill.

Most clinicians are firmly convinced that respiratory difficulties in the newborn are greater after Caesarean section than after delivery per vias naturales, but Craig and Fraser (1957), in a review of forty-nine neonatal deaths out of over one thousand patients delivered by Caesarean section in Aberdeen, found that in all but one instance the condition of the mother during the operation readily explained the baby's death. Nevertheless it would take more than figures such as these to convince us that pulmonary hyaline membrane disease is not more commonly provoked by Caesarean section and not coincidental as Craig and Fraser suggest. Admittedly, prematurity, diabetes and such antecedent circumstances as pre-eclamptic toxaemia and antepartum haemorrhage are all relevant factors, but our preference for delivering diabetic mothers by surgical induction of premature labour (and vaginal delivery wherever possible) has already rewarded us handsomely in the prevention of neonatal respiratory distress, as compared with the patients formerly delivered by elective Caesarean section.

IMMEDIATE TREATMENT

The child's first need is for oxygen to revive its vital centres. Neither the traditional methods of stimulation nor the administration of carbon dioxide is nowadays acceptable. Unfortunately you can take a horse to water but you can't make it drink and likewise you can administer oxygen to a baby but you have no greater certainty that it will breathe it.

Certain general principles are generally agreed. Firstly, the airway must be cleared by mechanical suction. The mouth-operated mucus extractors to be seen in so many old-fashioned labour wards are not only inefficient but make nonsense of all the other asceptic rituals in force. It is best to use a soft rubber catheter (size no. 4 French) with the end squarely cut off. A bevelled end to the catheter is useless because it tends to suck in mucous membrane, whereas a square-cut-ended catheter is free of this risk. It is important to insert the catheter into the back of the throat and also into the nostrils. The catheter is now pushed on downwards and the stomach emptied. This is particularly important after Caesarean section, and even more so after Caesarean section in diabetic patients, because of the amount of fluid which may be regurgitated from the stomach (Gellis et al., 1949).

Until both the nasopharynx and the stomach have been efficiently emptied the head is maintained tilted downwards and turned to one side to prevent the inhalation of any regurgitated material. After aspiration has been fully carried out it is better to prop the child up so as to take the weight of the liver off the diaphragm. Every anaesthetist knows how the Trendelenburg position in gynaecological surgery interferes with pulmonary ventilation, and the same applies to the newborn. The maintenance, therefore, of the

head-down position is illogical and harmful. It is irrationally thought by some that in addition to promoting drainage, the brain receives a better supply of blood in the head-down position, but nothing could be worse in the case of the asphyxiated baby whose cerebral blood vessels are already engorged to the point of rupture. In recognition of the shocked state, as described earlier, only the gentlest of handling is permissible. In the hope that the baby will presently take a gasp, oxygen is administered by face mask (which must not be too tightly applied round its face). A polythene type of funnel is very suitable for the purpose.

If it is suspected that the baby is failing to breathe satisfactorily because of previous administration of morphine, heroin or pethidine to the mother, an intravenous injection into the umbilical cord of 0.5 mg nalorphine is the next step. This should never be done empirically because more harm than good will be committed unless nalorphine is used as an antidote to these drugs. Nalorphine is not, by itself, a respiratory stimulant. For this reason it is sometimes better to administer nikethamide 0.25 to 0.5 ml intravenously first; although this drug has the disadvantage of being a convulsant and is likely to do more harm than good in the case of intracranial bleeding. The intravenous use of lobeline 3.2 mg as a stimulant to the respiratory centre is often helpful but its effect is transient.

All the time a watch is kept upon the vascular pulsation in the base of the umbilical cord. Any acceleration indicates success and encourages one to persist in the method already adopted.

At this point views diverge. One has the choice of doing nothing except maintaining a flow of oxygen in the region of the child's face, waiting for a spontaneous gasp, or of using some active method. We are in favour of tracheal intubation; nylon catheters without cuffs are particularly suitable for the purpose. Ill babies with flaccid muscles should be intubated without delay.

After preliminary suction positive pressure ventilation by intermittently squeezing a rubber bag up to a maximum pressure of 35 cm of water can be carried out. This will not expand the alveoli; it merely dilates the bronchioles, but guarantees that in addition to an airway the next breath the baby takes will be rich in oxygen. The phase of positive pressure must be as short as possible, not only to avoid interference with the filling of the right side of the heart but also to protect the few lung alveoli (which may already be opened) from expanding dangerously. High pressures, provided they do not operate for longer than 0.15 sec are less likely to damage the lungs (Day et al., 1952). This manoeuvre requires a certain degree of skill which is not always available, especially in the absence of an anaesthetist in the labour ward; its routine use is only feasible in the larger and better staffed units. A simple though far less effective alternative is to administer gastric oxygen. Two small catheters are passed down the oesophagus into the stomach, the second catheter being used to allow excess gas to escape. Oxygen is supplied via a Wolff bottle to ensure a safe but adequate flow. This treatment has enjoyed a great vogue in the last fifteen years. Some oxygen is absorbed from the mucous membrane of the gastro-intestinal tract, but it is doubtful if it is more than of marginal help; at least the technique calls for no special skill and is harmless.

Eve's rocking method has not received the attention it deserves. Although special mechanical rockers have been produced, the same effect can be satisfactorily obtained by holding the baby on one's arms and swinging the body through an arc from side to side as great as the state of the operator's vertebral column will permit, thereby using the weight of the child's liver on the flaccid diaphragm as a mechanical respiratory pump, and, even more important, to encourage venous return to the heart. The only disadvantage is the disturbance to the baby which it entails and the difficulty of administering oxygen at the same time. Mouth-to-mouth insufflation is still a widely practised and fairly satisfactory method in primitive circumstances.

None of these methods is as effective as intermittent positive pressure after endotracheal intubation, although Lord et al. (1953) do not favour this in the premature baby; we have not found it dangerous in even the smallest babies provided it is carried out very shortly after birth.

The question very naturally arises as to what pressures can safely be applied by artificial means to expand the lungs. The desirability of limiting the time of application of pressure to 0.15 sec

has already been mentioned, but even so there is clearly a limit to the safe height of the pressure employed. Using immediately excised lungs in the case of a fresh human stillbirth we have produced macroscopic evidence of damage at pressures exceeding 70 cm of water (Donald and Lord, 1953). We therefore avoid exceeding 35 cm of water, but Goddard (1955) uses intermittent positive pressures of 50 to 60 cm of water for the first twelve to twenty-four impulses taking care, however, to keep the flow time short, Thereafter he drops the pressures. He only intubated 10 per cent of his patients and reckoned that he achieved just as good pressure impulse patterns with a well fitting mask. Spontaneous pneumothorax (fig. 1) is by no means uncommon in otherwise healthy babies and the risk of inducing traumatic pneumothorax and mediastinal and interstitial emphysema must not be overlooked when considering mechanical methods of artificial separation. There is not a very wide margin between effective and dangerous pressures.

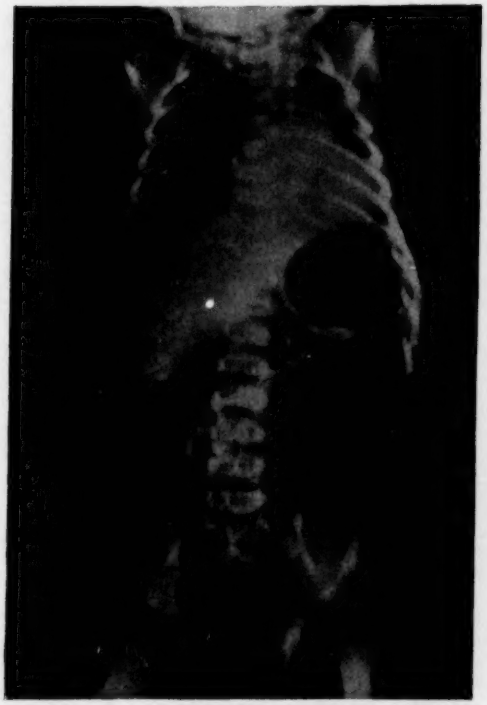

FIG. 1

Spontaneous bilateral pneumothorax as a cause of respiratory difficulty in the newborn. No method of artificial respiration has been employed.

AUGMENTED RESPIRATION

For the reasons previously stated we have developed the technique of augmented respiration, using an apparatus whose main activity synchronizes with the onset of the baby's inspiratory activity. By these means it is possible to keep the pressures applied to the minimum since they are summated with those of the baby's own respiratory effort and, secondly, the apparatus does not hinder the child's efforts by operating in antiphase with it. We have produced a number of such machines, aiming progressively at increasing simplicity of operation and portability. Our standard trigger mechanism is a photo-electric device operated by the onset of each spontaneous inspiratory flow. In the absence of spontaneous respiration a preset frequency of delivery automatically operates but cuts out in favour of augmenting spontaneous respiration as soon as it occurs. The principle at least would appear to be physiologically sound, inasmuch as the baby controls its own machine. We know it to be safe in an experience approaching two hundred patients and it is certainly a very quick way of getting oxygen into a distressed baby.

So often, however, one is endeavouring to salve the impossible, and the baby that has defied all the earlier methods of resuscitation is more often than not suffering from some mortal disorder. The disappointment rate from such treatment is consequently very high. The earlier our respirators are used the more likely is a successful result to be achieved, not simply because of the merits of the treatment, but because occasional patients would be included in the series that might have been capable of spontaneous recovery without it. This is the sort of thing that makes a statistical evaluation of its worth very difficult. Recently by chance, however, we had, through a mistake, an opportunity of illustrating the effect of one of our respirators on one lung and not on the other in the same baby. A fine endotracheal tube had been passed down too far and had entered the right bronchus. The child, the seventh

of an unfortunate woman who had lost all previous six babies under similar circumstances, had been delivered prematurely by elective Caesarean section and was very soon in desperate respiratory straits. It looked as though a seventh tragedy would be repeated, so the baby was intubated and treatment by augmented respiration begun. The child's condition steadily improved and after a few hours a radiograph was taken (fig. 2) and, to our dismay, it was seen that full or rather overfull aeration of the right lung had occurred as compared with almost total atelectasis of the left. The general condition of the baby, however, was by now very much fitter, and within the next few hours the left lung expanded as well, and the child has since thrived.

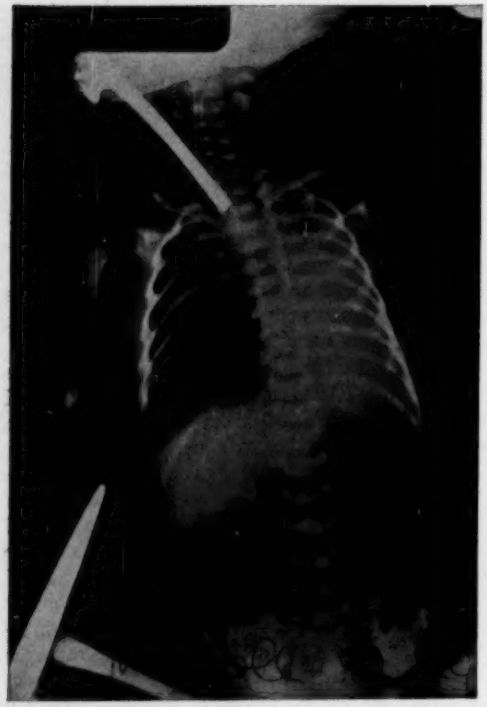

FIG. 2

A premature neonate treated by intubation and augmented respiration. The catheter has been passed too far and has entered the right bronchus. As a result the right lung is over-aerated and the "untreated" left lung still collapsed.

FAILURE TO MAINTAIN RESPIRATION

This is almost as important a subject as failure to initiate respiration at birth, but more directly concerns the paediatrician than the obstetrician or anaesthetist. Prematurity in association with the pulmonary syndrome of the newborn remains the most serious cause of neonatal death. This syndrome has been described by Bound et al. (1956) as resorption atelectasis together with hyaline membrane or intrapulmonary haemorrhage or pulmonary oedema. It is as well to mention that the circumstances attending a baby's birth, not forgetting the type of anaesthesia, are often impugned as causes of this distressing condition in which a baby may leave the operating theatre breathing and crying well only to succumb within the next forty-eight hours or so with lungs practically solid. The cause, however, is still under dispute, except that prematurity is regarded as a principal predisposing factor. Unfortunately space here precludes a fuller discussion of this important condition.

LATE EFFECTS OF ASPHYXIA NEONATORUM

Prolonged asphyxia at birth is generally regarded as capable of causing cerebral palsy, mental backwardness, behaviour disorders, and epilepsy, so that one often wonders what kind of future lies in store for the baby whose entry into the world has been so hazardous. No one would suggest that anoxia ever did the central nervous system any good and elsewhere I have stated my belief that every cyanotic attack is another nail in the coffin of the child's intellect (Donald et al., 1958). However, Fraser and Wilks (1959) have carried out a careful follow-up of severely asphyxiated babies at birth, excluding those which were premature, and found that the picture was more reassuring with regard to the major disabilities, although they admitted that minor impairment might be relatively common. These were Aberdonian children (possibly not representative) but Baird (1959), likewise in Aberdeen, reported that in the case of 64 children (all aged 9 years attending a special school) the labours were normal in 57, and in only one was there an obvious causative relationship with neonatal asphyxia, in this case a difficult forceps operation with disproportion.

Other factors such as the social classes of the

parents, prematurity, bad genetic history and maternal antenatal disorders more than accounted for the handicaps of the other children. Drillien (1959) likewise pointed out that only 13 per cent of the prematurely born babies whom she studied were of average or more than average intelligence, and it would appear that the higher incidence of unfavourable socio-economic factors associated with prematurity as a whole may operate to the detriment of the child's intellectual chances.

This is the kind of investigation which is wanted on a mass scale to evaluate the ultimate prognosis of severe neonatal asphyxia and, although the picture may not be as bad as feared, there can be no doubt that the baby is fortunate indeed who comes into this world spontaneously, head first, with the occiput anterior, emerging from a recently ruptured amniotic sac, unhindered by maternal anaesthesia and shouting lustily before its heels leave the maternal perineum.

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ANAESTHESIA AND THE NEONATE

BY

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IT is generally accepted that the term "neonate" refers to the newborn infant during the first twenty-eight days of life. During the first part of this period anaesthesia and surgery are mainly necessary for congenital lesions. In the latter part of the period, however, acquired pathological processes may require treatment. The majority of operations have to be performed urgently and are essential for survival.

In a five-year survey of neonatal surgery in a city of half a million inhabitants, there were 211 operations on neonatal infants from a total of 122,600 operations of all types. A classification of this work appears in table I. The two conditions most frequently requiring surgery were hypertrophic pyloric stenosis and congenital oesophageal atresia (Wilton, 1959).

In 1905 Rotch and Ladd reported on two patients with pyloric stenosis, one of whom, aged 3 weeks, survived a gastro-jejunostomy. The anaesthetic report was brief—"operation under ether."

Gross (1953) quotes a mortality of 0.75 per cent from 1,199 operations for pyloric stenosis performed at the Children's Medical Centre, Boston, between the years 1939 and 1952. At least 35 per cent were done in the neonatal period and open-drop ether anaesthesia was preferred. According to Smith (1959c), this technique is still used.

Admirable though the results of Ladd et al. (1946) and Gross (1953) may have been in the field of pyloric surgery, it is in the problems of thoracotomy in the newborn that the greatest progress has been made in neonatal anaesthesia, and the results have subsequently been applied to anaesthesia for neonatal surgery in general.

In 1913 Richter described his attempts to treat two patients with congenital oesophageal atresia. Both operations were unsuccessful. An endotracheal ether-air mixture was given by insufflation to obtain positive pressure for pulmonary ventilation during thoracotomy. A pressure blow-off device was incorporated in the system.

It was not until 1938 that Leven (1941), and Ladd (1944) performed the first multiple stage operations resulting in long periods of survival. These operations required an extrapleural approach to the oesophagus.

TABLE I
Summary of neonatal surgery in a five-year period.

THORACIC SURGERY	
Oesophageal atresia	31
Diaphragmatic hernia	3
Tetralogy of Fallot	1
Thoracotomy for empyema	1
Lobectomy	2
Endoscopies	9
Miscellaneous	2
Total	49
ABDOMINAL SURGERY	
Ramstedt's	49
Exomphalos	11
Intestinal atresia	18
Meconium ileus	8
Herniorrhaphy	4
Laparotomy	4
Imperforate anus	4
Miscellaneous	5
Total	103
NEURO-SURGERY	
Meningocoele	18
Spina bifida	6
Ventriculography	5
Miscellaneous	2
Total	31
GENERAL AND PLASTIC SURGERY	
Micrognathos	15
Osteomyelitis	2
Amputation	1
Burns	1
Incision of abcess	3
Miscellaneous	6
Total	28

To Haight and Towsley (1943), however, must be given the credit for achieving the first successful direct primary anastomosis of the oesophageal segments. Here again, the approach was extrapleural, through a right posterior incision under local anaesthesia. The pleura was frequently opened where the struggling infant blew out the parietal pleura against the divided posterior ends of the ribs. Thus what had started as an extrapleural procedure became complicated by pneumothorax and paradoxical respiration. They recorded also that the crying of the infant pulled the oesophageal segments apart. The initial infiltration anaesthesia (0.25 per cent metycaine) had to be supplemented with positive pressure ether anaesthesia to subdue the vigorous reflexes of the struggling infant, and to overcome paradoxical respiration. No attempt was made to provide intratracheal aspiration of secretions. The complications of the pneumothorax, even though controlled by positive pressure, added greatly to respiratory embarrassment during operation. At that time it was assumed that an infant would be unable to stand a major intrathoracic procedure.

Singleton and Knight (1944) reported the first primary oesophageal anastomosis by the transpleural route. The operation was under "general anaesthesia", and at closure the "lung was expanded by intratracheal pressure".

Premedication

Premedication is given to neonates primarily for antisialogogue and vagolytic effects, and secondarily for sedation during operations under local anaesthesia.

Leigh and Bolton (1948) advocated the use of morphine, 0.14 mg for a 3.2–4.5 kg baby. It is now thought that morphine is contra-indicated in the neonate. Akin and Forbes (1947), reporting on 147 operations for hypertrophic pyloric stenosis, found that 8 patients developed cyanosis and respiratory depression in the post-operative period following local analgesia after morphine premedication. Induction with volatile or gaseous agents is retarded considerably following the use of morphine in the amounts suggested above.

Leatherdale (1958) advised the use of chloral hydrate as a sedative premedicant on the basis of chloral 130 mg/kg body weight.

Stephen and Slater (1949) suggested a suitable dose of atropine for a 3.2 kg baby would be 0.15 mg, or hyoscine 0.1 mg. On a dose-for-weight basis, both these would seem excessive. In practice these quantities prove satisfactory, as atropine has a wide safety margin, and the relatively large dose probably accounts for its efficient drying action in the newborn. Leigh and Belton (1950) suggest that atropine may be a factor in producing hyperthermia.

Nafe (1947) had used phenobarbitone 65 mg per rectum, half an hour before operation.

Numerous writers refer to the soporific effects of port wine or brandy for the child during procedures under local anaesthesia.

Intubation.

For many years there was a prejudice against endotracheal intubation in the newborn, in spite of the contribution of Ayre (1937) who reported his T-piece technique for infants undergoing harelip and cleft palate operations, which at that time were sometimes done in the first 24 hours of life (Botsford, 1935). Ayre also warned of the ease with which the endotracheal tube may become kinked in the pharynx or pass into one or other bronchus. This problem had been observed by Magill (1959), who designed his armoured endotracheal tube to overcome it in 1932. Alsop (1955) described an L-shaped tube in several sizes, the smallest of which was suitable for infants and neonates; this tube was planned to obviate the danger of obstruction to respiration by kinked tubes. Cole (1945) noted that intubation was often avoided because of the narrowness of the tube that must be used with its consequent resistance to breathing. He designed a new endotracheal tube to overcome this difficulty. Chandler (1958) pointed out that respiratory obstruction could occur with certain types of Magill flexometallic tubes when a high flow rate of fresh gases was projected down the narrow side tube against the expired gases from the infant.

Gillespie (1939), made a plea for endotracheal anaesthesia in infants, although he referred particularly to infants over 6 weeks of age. He described the Shadwell laryngoscope to facilitate intubation in the infant. The infrequency of operations on the neonate afforded only a few anaesthetists the opportunity of obtaining experi-

ence in handling them. This factor added to the inherent difficulties of intubating these infants and delayed the more general application of this technique. Lam (1946) stated that he believed the oesophageal anastomosis in congenital oesophageal atresia could be made immensely easier "if the patient were receiving general anaesthesia through an intratracheal tube, the so-called controlled respiration method", though his wholehearted advocacy was tempered by damage to trachea and lungs following prolonged and repeated intubation as reported by Cassels and Yeager (1945).

Stephen and Slater (1949) listed the advantages of intubation as follows: the airway is assured; operations on the head and neck are safely performed; suction of the trachea is facilitated; a lighter plane of anaesthesia can be used and in operations on the open thorax, control of lung ventilation is facilitated.

Roberts (1950), writing of his experiences of 8 patients with congenital oesophageal atresia, advocated intubation and controlled respiration with the use of relaxants to overcome the dangerous paradoxical respiration which develops, even in the extrapleural operation, if the child is allowed to breathe spontaneously.

Leigh and Bolton (1950), referring to the dangers of regurgitation in infants with intestinal obstruction, advise intubation, and state "intubation of all oral, nasal, head, thoracic or abdominal operations with the patient in the prone position, appears to have merited recognition and practice". If laryngitis occurred postoperatively it could be observed immediately on extubation.

Rees (1950) and Wilton (1951) in two papers devoted solely to problems of neonatal anaesthesia reported on the advantages of intubation, particularly with reference to endotracheal suction, efficient gaseous exchange and oxygenation. The physiology of the neonate is discussed fully by Rees, and the benefits of controlled respiration to the immature respiratory system are described and justified. In these papers both writers agree that intubation is essential where controlled respiration is employed. Intubation is performed after induction of anaesthesia. Rees refers to the difficulty of intubating the neonate because "the infant larynx occupies a higher position in the neck in relation to the vertebrae, and the axis of its lumen tends to pass forwards as well as downwards." The value of the shoulder on the old type of Magill armoured tube to prevent the tip passing into a bronchus was pointed out by Wilton, who advised trimming back to a length of half an inch, that portion of the tube which was to pass beyond the cords.

Eckenhoff (1951) noted the increased use of endotracheal techniques in children. He reported that 98 per cent of all infants of less than 2 weeks were intubated. He believed the advantages far outweighed the disadvantages. The importance of laryngeal oedema was stressed. Owing to the encirclement of the cricoid cartilage the aperture here was smaller than at vocal cord level and was unyielding. Quoting Holinger and Johnston (1950), he pointed out that, if the area of the air passage at the cricoid ring in an infant was 14 sq.mm, then 1 mm thickness of oedema would reduce this area by 65 per cent.

Gross and Ferguson (1952), in a report of surgery on 159 premature infants, stated that they did not like to intubate and inflate them, because of the danger of over-distension of the lungs, with the subsequent development of pulmonary oedema.

Discoursing on the prevention of tracheitis in children following intubation, Smith (1953) suggests that infants have an increased susceptibility to infection of the larynx, which is indicated by a high incidence of primary laryngotracheitis. He lists several causes of tracheitis, such as the use of heavy laryngoscopes, use of force to intubate, chemical irritation, sepsis, inadequate relaxation and contaminated lubricants. Blind nasal intubation should be used only for specific indications. Laryngeal oedema should be treated with antibiotics, oxygen and humidification.

Zindler and van Deming (1953), in a review of the anaesthetic management of 49 patients with congenital oesophageal atresia, recommend that the external diameter of the endotracheal tube should not be more than 4.6 mm, and that as unusually sensitive laryngeal reflexes make ordinary methods of induction tedious, intubation should be performed before induction. Macintosh (1940) advised the application of 10 per cent cocaine on the tip of the finger to the cords

during induction. This considerably reduces the laryngospasm, which is normally only overcome with deep anaesthesia.

It is now an accepted practice to intubate the neonate, with or without the aid of a short-acting relaxant before anaesthesia is commenced.

Smith (1954) reviewed the advantages and disadvantages of endotracheal anaesthesia. Although not specifically referring to neonates, the principles still apply. He divided operations into four categories in the first of which intubation is mandatory These are intracranial and intrathoracic procedures, major operations in prone position, operations in the presence of intestinal distension, operations after recent feeding.

In a second group intubation is preferable. Patients with pyloric stenosis fall into this class. If the gastric contents are fluid, and can be aspirated through a Levin tube, then this short operation can safely be performed without intubation. If curds and solids are present, intubation is desirable. Intubation is optional for lower abdominal operations, and is unjustified for minor surgery.

When skilfully performed, endotracheal intubation of the neonate must be considered to be not only a great safety factor but an essential component of most of the usual techniques in use. Prejudice has been overcome, and the position now is as described by Cope (1956), "oral intubation with an uncuffed tube for every case at any age undergoing abdominal surgery has become standard practice with us". He intubates with the aid of a short-acting relaxant, and attributes the lack of laryngeal oedema in recent practice to the atraumatic intubation. He warns against the use of the relaxant where there is any chance of a full stomach or regurgitation.

Inflating an apnoeic and curarized infant by bag and mask can be dangerous, and it is on record that this technique has resulted in oxygen passing down the oesophagus, and out through the entire line of an oesophageal anastomosis, resulting in a bilateral pneumothorax.

Extubation must be undertaken with caution, and spontaneous respiration should be fully regained before removing a tube. The pharynx should be sucked out under direct laryngoscopic vision, and the trachea aspirated with a fine polythene tube which should pass easily through the endotracheal tube without occluding the lumen. The tip of the endotracheal tube should leave the larynx when the chest is in full inspiration, and poised to cough out any remaining secretion or blood clot.

Zindler and van Deming (1953) administered a mixture of carbon dioxide, oxygen and helium just prior to extubation, to fill the lungs with a less diffusible gas, as a means of preventing atelectasis.

Relaxants.

The prejudices against intubation had their parallel with reference to the use of relaxant drugs. The occurrence of prolonged apnoea and paralysis following the use of non-depolarizing agents (Roberts, 1950) occurred more frequently than the literature would lead one to believe.

During an operation for diaphragmatic hernia in a 2-weeks-old infant, under an ether-oxygen anaesthetic, Griffith (1943) reported that 20 mg of d-tubocurarine were given in error. He noted that excellent operating conditions resulted, and that following 3½ hours of artificial respiration through an endotracheal tube, complete recovery took place.

Two operations for pyloric stenosis were described by Cullen (1943), where local infiltration of the abdominal wall by procaine had produced inadequate relaxation. Cullen administered small doses of d-tubocurarine intravenously, without assisted respiration, and obtained sufficient relaxation for the atraumatic and easy replacement of the bowel into the abdominal cavity.

Intocostrin and d-tubocurarine were used as the sole agent of anaesthesia and relaxation by Smith (1947) in a series of 41 patients, about 30 per cent of whom were neonates. No attempt at aided respiration was made and intubation was only performed if complete respiratory arrest occurred. If relaxants are used to a degree where respiratory exchange is impaired, controlled or aided respiration is essential. This principle applies most especially to the neonate. Rees (1950) and Wilton (1951) both agreed that the use of relaxing agents in the newborn were unnecessary and dangerous. These writers stated that for thoracotomy, controlled respiration was easily obtained with the use of hyperventilation and minimal ether. At that time only the non-depolarizing relaxing agents were available.

Gallamine and d-tubocurarine remained the usual relaxants in use for some years. Fairlie (1954, 1959) preferred the former because of its shorter action, and used doses in the order of 2.2 mg/kg body weight. Lucas (1959) was using d-tubocurarine in 1951 and continues to do so, having found this drug entirely satisfactory in doses of 2.2 mg per 10 kg body weight. He has not exceeded 1.5 mg total dose, and the initial dose is usually 0.5 mg.

Payne (1955) used d-tubocurarine in amounts of 0.55–1.1 mg/kg body weight in a 2.5 per cent solution, followed by increments of 0.45 mg/kg body weight. For reversal of curarization he advised the use of neostigmine 65μg/kg* body weight preceded by atropine 0.3 mg.

Recently Stead (1955), in a review of 300 neonatal operations showed that the response of the newborn infant to relaxant drugs differed from that of the adult. The neonate needs at least twice the dose per kg body weight of suxamethonium to produce comparable results. There exists an increased sensitivity to d-tubocurarine in the neonate, and extreme care must be exercised in its use. Rees (1950) stated that he thought it doubtful if a reliable reversal of d-tubocurarine could be obtained in the neonate. Stead (1955) advised the use of suxamethonium in doses of 5 mg repeated up to a total of 15 to 45 mg. In spite of the lower pseudo-cholinesterase levels known to exist in neonates, no prolonged apnoea was encountered. The writer of an annotation (1955) warned that a late competitive type of block might follow large doses of suxamethonium in the newborn. If suxamethonium is to be used intermittently, Rees (1957) states that incremental doses must be kept as low as 1 to 1.25 mg. This agent is hydrolyzed in vivo to succinylmonocholine, which also can produce a neuromuscular block. As there may be some dual block ether should be avoided. Bryce-Smith (1959) also emphasizes the dangers of dual block occurring, and in long operations after an initial large dose of suxamethonium, he maintains controlled respiration by the addition of small amounts of ether or halothane.

The use of relaxant drugs in cardiovascular surgery in children is referred to by Telford and Keats (1957). Suxamethonium is given in 5 per cent dextrose in water as a 0.2 per cent solution. Light ether anaesthesia is preferred for maintenance.

Hellings et al. (1958) report a series of 54 operations for oesophageal atresia in which they used a technique of relaxant and nitrous oxide. A careful system of assessing the dosage of suxamethonium is suggested; the total should not exceed 50 mg. In the event of difficulties with the intravenous route, McDonald and Bryce-Smith (1955) showed that suxamethonium may safely be given intramuscularly, with or without hyaluronidase.

Local anaesthesia.

With the application of relaxant drugs, intubation, controlled respiration, and general anaesthesia in neonatal surgery, the field of use for local anaesthesia has diminished considerably. This technique is not without danger, and intoxication has been reported. In an account of 100 operations for pyloric stenosis, Ward-McQuaid and Porritt (1950) quote two examples of overdosage with 1/1000 cinchocaine. Ten of their patients required supplementary general anaesthesia. Leatherdale (1958) in his series of 150 operations for pyloric stenosis, used various drugs (cinchocaine, lignocaine, and procaine). He stressed the importance of adjusting the dose to the body weight. Two infants had convulsions from overdosage and were given thiopentone and oxygen.

Straith et al. (1955) and McCash (1957) prefer local anaesthesia for cleft lip surgery in patients undergoing operations during the first ten days of life.

In neurosurgery, local anaesthesia (0.25 per cent lignocaine and 1/200,000 adrenaline) is mainly used in the repair of a meningocoele that is about to rupture (Brown, 1959).

Prematurity.

A useful working definition of the term is given by Gross and Ferguson (1952), who regard all neonates weighing less than 2.3 kg when operated on as premature, regardless of the gestation period.

Smith (1959b) remarks that prematurity is one of the greatest threats to survival. According to Tyson (1943) the survival of a premature

*N B. 1 μg$=\frac{1}{1000}$mg.

infant may also depend on whether or not the mother has received morphine during labour. Roberts (1949), quoting Assali and Zacharias, showed that of 673 neonatal deaths following 15,088 births, 49.5 per cent were due to prematurity. It is not surprising, therefore, that these patients represent some of the poorest material in paediatric surgery.

Gross and Ferguson (1952) review 159 operations on premature infants. In a discussion of the physiological problems involved, they suggest that the premature infant's respiratory inefficiency is compensated for by a greater respiratory rate, and greater physical effort. If respiration is hampered by intestinal distension or a diaphragmatic hernia, there is little pulmonary reserve. There is little cardiac reserve either, and as such infants also lack adequate peripheral vasomotor control, there is a particular susceptibility to succumb to relatively slight blood loss. There is, too, a tendency for hypoprothrombinaemia to develop.

No hard and fast rules can be laid down for the most suitable agents or techniques for anaesthetic use upon these infants. The type of operation, and the general condition of the patient must be taken into consideration. For example, local anaesthesia does not necessarily afford the safest means of providing relaxation for reducing a large omphalocoele in a shocked premature 1.8 kg baby; some relaxant may be required. Relaxants must be used with care and accuracy. Prematurity in itself is not a contra-indication to intubation. Indeed, intubation and gentle expansion of the lungs by positive pressure may be an important aid to resuscitation. It has been found that premature infants of even 1.6 kg stand thoracotomy well if intubated, and inflated with nitrous oxide-oxygen and minimal ether. Closely following the associated congenital heart lesions, the greatest menace to the premature infant is its inability to cough effectively. Bronchoscopy may therefore be life-saving, and atropine is best omitted in premedication because of its tendency to increase the viscosity of bronchial secretions.

Temperature.

Opinion concerning the optimum temperature for neonates during surgery is not yet conclusive. The premature infant is particularly unstable, and tends to take up the temperature of its environment. Louw et al. (1954) consider that premature infants should be kept in a temperature of 90°F until the body reaches 97°F. The environmental temperature should then be reduced to 80–85°F to allow the infant to establish its own temperature, which is usually 96–98°F.

The possibility of reducing the infant's oxygen demands by lowering body temperature was stated by Silverman (quoted by Smith, 1959a) to be inadvisable, and to have contributed to an increased mortality.

In an investigation of the body temperatures of a group of 215 children (10 of whom were neonates) undergoing operation, Bigler and McQuiston (1951) found that most infants under 6 months of age developed hypothermia, which the writers did not consider harmful. This finding is corroborated by Hellings et al. (1958) and emphasized by Rickham (1957), who states that allowing the temperature to fall, often to 85°F, "has greatly facilitated anaesthesia and postoperative recovery".

Bering and Watson (1953) considered that severe hypothermia was harmful, and used an electric blanket. Where severe hypothermia had been prevented during neurosurgical operations, postoperative recovery was accelerated.

The causes of hypothermia have been listed by Leigh et al. (1956) who suggested that cooling an overheated patient would increase the chances of survival. Cooling to 82.4°F was safe, providing arterial oxygen saturation was maintained, and might be applied with advantage to cyanotic infants who must undergo extrathoracic surgery.

Agents and techniques.

Since Lundy (1924) published his observations on the use of ethylene a perusal of the literature reveals the not unexpected situation that almost every anaesthetic agent has at one time or another been applied to the neonate.

Some anaesthetists consider that the newborn baby does not require an anaesthetic, as he is not a conscious being, and does not appreciate pain (Lucas, 1959). These views are supported by the opinion of McGraw (1943), who states that "it is generally agreed that the sensitivity threshold of the newborn infant to externally

applied stimuli, is high". Robson (1925) described this practice as "vivisection".

Diverse as are the agents and techniques in use, certain principles have become established in clinical practice. The long accepted opinion that infants could withstand oxygen lack without sequelae is no longer tenable (van Deming, 1952). The importance of reducing deadspace in apparatus, and efficient elimination of carbon dioxide has been recognized by numerous writers, and several nonrebreathing valves have been described. According to Slater and Stephen (1951), "In infants a few days old undergoing major procedures, the endotracheal nonrebreathing method is employed by preference." The use of closed circuit absorption apparatus was condemned by Leigh and Belton (1950). The importance of lack of resistance to respiration was recognized by Ayre (1937) who states that: "the open endotracheal technique enables the most weakly infant to breathe under normal physiological conditions". These principles have been adapted to the neonate in the form of "balanced anaesthesia", as they are in the adult. Intubation, relaxants, semi-closed circuits, with or without absorbers, controlled respiration, and the use of nitrous oxide-oxygen mixture delivered at relatively high flow rates, for analgesia, are standard practice today.

Rees (1958) stresses the importance of maintaining controlled respiration at a high rate to overcome the physiological and mechanical deficiencies of the neonate's immature respiratory system.

There should be no hesitation on the part of the anaesthetist who meets these problems infrequently to resort to the use of ether, an agent which has so frequently been described as the safest anaesthetic in paediatric surgery. The absence of an opiate premedication, and the minute quantities of ether required in the neonate, are factors which allow a rapid return to consciousness not seen in the adult patient.

Halothane is still in the probationary stage as far as the neonate is concerned. This agent has been used in a small series by Evans (1959), mostly for thoracotomy, and for the Fredet-Ramstedt operation. Control of respiration was easily obtained, satisfactory operating conditions were provided, and the majority of patients had active laryngeal reflexes when they were extubated.

Bull et al. (1958) warn that halothane produces respiratory depression and hypotension in infants. Two per cent halothane is inadequate where much muscle relaxation is required. Increasing the concentration improves the relaxation, but is accompanied by a fall in blood pressure. The writers therefore recommend that, rather than increasing the concentration, resort should be made to a relaxant, and controlled respiration.

Special cases.

Micrognathos. In patients with the Pierre-Robin syndrome the lower jaw is underdeveloped and acute attacks of upper respiratory obstruction occur when a relatively large tongue impacts in the cleft palate (fig. 1). Douglas (1956) showed that by suturing the tongue to the lower lip the

FIG. 1

Illustration of gross underdevelopment of the mandible in the Pierre-Robin syndrome

mortality could be very considerably lowered. Intubation of these infants is essential to provide safe operating conditions (Routledge, 1959). Laryngoscopy and intubation can be a difficult procedure, due to the cleft palate and receding lower jaw. These infants should be intubated without relaxant drugs or anaesthesia. When the tip of the laryngoscope has reached the vicinity of the glottis, gentle pressure with one finger over the thyroid cartilage will bring the cords into view.

Congenital cystic disease of the lung. These infants also present as acute respiratory emergencies. The cystic lobe or lung inflates, but cannot deflate. The patient arrives at operation with gross mediastinal shift to the healthy side. Cyanosis with tachypnoea results from compression of the normal lung between cystic lung and chest wall. These patients should be allowed to respire spontaneously following intubation. Any attempt at positive pressure inflation will only increase the distension of the cystic portion, and will aggravate the compression of the heart and great vessels. Pulmonary reaction is not usually difficult in these patients, and is quickly accomplished. Not until the bronchus is clamped, and the cystic portion is freed, should controlled respiration be instituted, and the healthy lung expanded.

Pre-operative preparation and postoperative care. It has been stated, that setting up a blood transfusion is the most important step in an operation for congenital oesophageal atresia. Many writers put forward suggestions on the quantity of blood required. Rickham (1945) considers that the colorimetric technique is the only reliable method for estimating blood loss. He considers that blood replacement should be based on a calculation of blood loss. Slight over-transfusion has been effective in lowering operative mortality.

Louw et al. (1954) report at some length their conclusions on the correction of electrolyte imbalance. Infants cannot excrete salt easily, and sodium chloride must be given with extreme care. The basic daily requirements of the neonate is 0.25 g. sodium chloride.

The pre-operative correction of dehydration and alkalosis due to vomiting in pyloric obstruction, has been a major factor in lowering mortality in that condition.

Postoperative complications are not infrequent, and often require urgent attention. The neonate should be nursed in an atmosphere of 100 per cent humidity, and if the secretions are very tenacious a mucolytic agent should be added (De Boer and Potts, 1957). Infants should be turned from one side to the other every hour. Cardiac arrest has been known to occur ten times in one infant. Cardiac arrest occurring postoperatively should be treated by cardiac massage through an upper abdominal incision. This can be closed easily by clips, and can be reopened quickly if another arrest occurs (Belsey, 1959).

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PREMEDICATION OF CHILDREN FOR SURGERY

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THE child is not a diminutive adult but an immature organism with anatomical, physiological and psychological features peculiar to his age. These features change continuously throughout life and the most rapid change occurs in the first decade.

The most satisfactory results are obtained from premedication when the anaesthetist is aware of these differences and makes adjustments accordingly. To have a "routine" premedication for adults before a certain surgical procedure is practicable but not ideal; in infancy and childhood, it is rarely satisfactory because premedication should vary with the type of operation, the age of the child, and with his physical and psychological make-up. For this reason premedication must be considered with the preoperative assessment and care of the child. Fortunately the days are passing when the anaesthetist first meets his patient in the anaesthetic room. A visit by the anaesthetist, not later than the day before operation, is even more important for children than for adults, The physical and emotional condition can only be assessed by seeing the patient, when the most suitable premedication can be selected.

PRE-OPERATIVE EXAMINATION

Psychological assessment.

The care of the child before operation is part of the general problem of care of children in hospital. Children are more vulnerable than adults to emotional stresses and a child is often terrified at being removed from his parents to a hospital; a place of strangers. Whereas adult distress in hospital is more likely to result from the fear of illness, death, and loss of livelihood and from worries about the welfare of his dependants. The ability of the child to adapt to hospital life depends on his inherited personality and how he has been reared. Age is an important factor too, for as a rule the younger the child the more difficult the adjustment will be. The emotional relationship between the child and his parents, their manner of preparing him for hospital admission, and the nature of ordeals experienced once he is in hospital, are all factors which will influence his reaction. The nursing and medical staff should aim to make the hospital visit a happy memory, leaving no dread of returning in the future. The child should be told, if old enough to understand, the reason for being in hospital, and on no account should promises be made which are not fulfilled. Children under the age of five years have not reached a stage of development necessary for understanding and may react very badly to hospital admission. Premedication and anaesthesia should therefore be arranged in such a way as to avoid unpleasant memories. After the age of five or six, a child whose mental and emotional development is normal, will usually be able to understand why he is going to hospital, and that the separation from home and parents is only temporary. A brief description of the anaesthetic technique will make the task of the anaesthetist much easier. Older children can be regarded as adults when assessing premedication and subsequent anaesthetic technique.

Physical examination.

Symptoms. Physical examination of the infant and small child presents greater problems and is more time consuming than in the adult. The young patient is unable to provide a history for himself, and the anaesthetist must rely on information obtained from the parents or nursing staff, as well as his own observations. Trivial symptoms in children must be regarded with suspicion, for they may herald an infectious illness which would contra-indicate anaesthesia and surgery in all but emergency procedures. When there is doubt in the anaesthetist's mind

concerning the fitness of the child for elective surgery, then the operation should be postponed. Cough, nasal discharge, vomiting, loose stools, or fever, must be investigated and treated before surgery is undertaken. Sometimes a raised temperature recorded on admission to hospital may be caused by apprehension or excitement, but if above 100°F, or persisting overnight when the child is sleeping, then some other cause must be sought. A particularly difficult problem is presented by children admitted for surgery of the ear, nose and throat. These patients often have chronic nasal or aural discharge or a cough, which will clear only after the necessary operation. Nevertheless the anaesthetist must decide whether a fresh infection has occurred. If the child has chronic cough or is "wheezy" it may be considered wise to postpone the operation for a few days, so that the patient can benefit from physiotherapy and a course of antihistaminic and antibiotic drugs.

The haemoglobin of all infants and children should be estimated as a routine before major procedures and of any patient who appears pale and anaemic. A level of *at least* 80 per cent of the normal haemoglobin expected for the age group should be reached before surgery is undertaken. A course of iron or, in severe anaemia, a blood transfusion may be required before operation; and in all cases of major surgery blood must be grouped and cross-matched for use during the operation. Infants withstand blood loss poorly. Assuming the normal circulating blood volume to be 89 ml/kg (40 ml/lb.), a 4.5 kg (10 lb.) baby has to lose only 40 ml to lose one-tenth of his total blood volume (equivalent to over 0.5 litre in the average adult). Infants with hare-lip and other feeding difficulties are particularly likely to be deficient in haemoglobin, and frequently require a course of iron before operation.

Physical signs. The examination of the patient should include the respiratory and cardiovascular systems. Obstruction in the nose, pharynx, and larynx which might lead to difficulty during anaesthesia should be looked for; and it is a wise precaution to record the presence of loose teeth. Veins suitable for the induction of anaesthesia should be sought for, because the type and amount of premedication is determined to a certain extent by the accessibility of veins for this purpose. The physical and mental development of the child also has an important bearing on the premedication.

PRE-OPERATIVE PREPARATION

When the child has been declared fit for surgery, consideration is next given to the preparation for operation which will include the choice of drugs for premedication. Children seldom require a sedative on the night preceding operation, for they usually sleep well. If an older child seems unduly apprehensive, a barbiturate or phenothiazine drug can be given to promote sleep.

Feeding. Young children may retain food in the stomach many hours after a meal and also tolerate water deprivation badly. Their daily intake and output of water is greater than in the adult, yet their water reserves are proportionately smaller. Nutrition of the child in the pre-operative period presents greater difficulties than in the adult. On the one hand it is important to avoid ketosis and dehydration to which the young child is particularly prone when carbohydrate and fluid intake is restricted: yet equal care must be taken to avoid regurgitation of stomach contents during the induction of anaesthesia. No solid food should be given for *at least* four hours before the induction of anaesthesia; but sips of sweetened water can be given up to two hours before operation. Sweetened orange squash is not recommended as it is sickly and tends to encourage vomiting.

Drug therapy. Drugs prescribed as part of the child's treatment programme are best given by injection during the pre-operative period. There is then no danger of regurgitation of a drug which may have special therapeutic importance. The same precautions regarding patients who have been receiving cortisone must be observed for children as for adults in the pre-operative period.

Bowel management. This should never include strong purgation which may cause dehydration. Bowel washouts are not recommended before rectal narcosis because they are unnecessary and may irritate the rectum, causing the drug to be returned. With an operation in the morning a suppository or enema should be given not later than the night before.

Clothing. The child's covering should be as light as possible to avoid fluid loss from sweating.

Woollen blankets and clothes are harmful because they carry the risk of spark production as well as overheating. The child should arrive in the anaesthetic room cool and comfortable, with his metabolic rate and oxygen requirements not raised unnecessarily by measures which have prevented heat dispersal.

The newborn provide an exception to this rule. The metabolic rate is low at birth, and the newborn have imperfect temperature regulation. They are rarely seen to shiver and tend to lose heat rapidly. To avoid this the newborn should be wrapped in cotton wool or gamgee during the induction of anaesthesia and throughout operation.

PRE-OPERATIVE MEDICATION

The drugs given in the pre-operative period can be divided into three groups: (1) parasympatholytic; (2) antihistaminic; (3) sedative, hypnotic, and analgesic.

(1) PARASYMPATHOLYTIC

Drugs of the belladonna group are included in the premedication on account of their depressant effect on the parasympathetic division of the autonomic nervous system. The choice of drug usually lies between atropine and hyoscine. Drugs of this group produce effects which are both helpful and unhelpful to the anaesthetist, but it is generally agreed that the advantages outweigh the disadvantages.

The beneficial effects are as follows:

(*a*) There is a reduction of secretion of mucus and saliva from the mouth, stomach and tracheobronchial tree. To keep the airway free from mucus is even more important to infants than adults, for infants secrete mucus readily, yet their normal airway is very small. Hence only a small blob of mucus may lead to obstruction of the airway and the development of dangerous anoxia. The author has found that atropine is a more potent "drying" agent than hyoscine.

(*b*) Another advantage offered by these drugs is a vagolytic action. By paralyzing the vagal nerve endings in the heart these drugs will afford protection against cardiac slowing or syncope caused either by mechanical stimulation or by anaesthetic agents such as suxamethonium or halothane. Atropine is superior to hyoscine as a vagolytic agent in the doses usually employed.

(*c*) Hyoscine has a central depressant action, which is obvious only when used in combination with the opiates or pethidine.

The disadvantages of these drugs are:

(*a*) Sweating is reduced by both drugs. This may provoke hyperthermia and convulsions. To prevent this the dose of atropine or hyoscine should be reduced in children with a high fever, or when the theatre temperature is very high. Furthermore the inhibition of secretory activity depresses ciliary action in the respiratory tract.

(*b*) Atropine is a metabolic stimulant. This will counteract to a certain extent the hypnotic effect of the opiate and increase the oxygen demand by raising the metabolic rate.

(*c*) Tachycardia is produced by these drugs, but more so by atropine than hyoscine. This can be a disadvantage in a child who already has a fast pulse rate. The choice of drug is determined ultimately by the personal preference of the anaesthetist.

Extensive trials by the author, of both atropine and hyoscine used alone and in combination with other drugs, gave the impression that hyoscine is satisfactory only when used in combination with the opiates or pethidine. When used alone, doses of hyoscine as high as 22μg/kg* (0.01 mg/lb.) fail to produce a dry respiratory tract or a sedative effect; yet 11 μg/kg (0.005 mg/lb.) produces a very satisfactory drying and sedative effect when given with the opiates or pethidine (Anderson, 1952).

Dosage of parasympatholytic drugs.

The recommended dosages of atropine and hyoscine for children are: atropine 44 μg/kg (0.02 mg/lb.) reaching a maximum of 0.6 mg at 13.5 kg (30 lb.); hyoscine 13μg/kg (0.006 mg/lb.) reaching a maximum of 0.4 mg at 31.5 kg (70 lb.).

For the best results these drugs are administered by intramuscular injection rather than by mouth or rectum. In an emergency, however, atropine can be given intravenously for rapid action.

Contra-indications for the use of atropine and hyoscine.

The dose of atropine and hyoscine should be reduced in children who have a high fever and

*N.B. $1\ \mu g = \frac{1}{1000}$ mg.

also in hot weather if the theatre is not air-conditioned. Neglect of this predisposes to hyperthermia with a consequent increase in the metabolic rate and to other hazards already mentioned.

(2) ANTIHISTAMINIC DRUGS

This group of drugs, mostly phenothiazine derivatives, in addition to antagonizing histamine, produce sedation as a side effect. They have valuable anti-emetic and potentiating actions.

(a) *Promethazine.*

This is at present the most useful of the phenothiazine drugs to the anaesthetist. It can be given by mouth or by injection and may be selected for sedative, anti-emetic and antihistaminic properties.

Because its antihistiminic action prevents bronchoconstriction, promethazine is particularly valuable for premedication when chronic bronchitic or asthmatic patients come to surgery. The drowsiness which follows its administration is not accompanied by respiratory depression or cardiovascular disturbance. Combined with other drugs promethazine is proving as valuable for premedication in children as for adults. The dose is 1.1–2.2 mg/kg (0.5–1 mg/lb.) body weight.

The author has noticed one sequel to giving promethazine with papaveretum and hyoscine to children which has not been observed in adults. A child may be peacefully sleeping after this premedication; but when disturbed to be lifted on a trolley, or to receive an injection of thiopentone, he may become wildly excited, throw his arms about, and shout as though in a nightmare. Memory of the episode, however, is not retained.

(b) *Trimeprazine tartrate.*

This is a recently developed phenothiazine derivative which has strong antihistaminic and anti-emetic properties (Cope and Glover, 1959). Trimeprazine tartrate is only available for oral administration and therefore carries all the disadvantages of this route for premedication.

(c) *Chlorpromazine.*

Chlorpromazine has very little antihistaminic action. The tachycardia and vasodilatation produced as side effects are particularly unwelcome in childhood because infants and young chidren normally have a high pulse rate. Chlorpromazine does not inhibit secretory activity well enough to make a belladonna drug entirely unnecessary before general anaesthesia. This is an important disadvantage because atropine likewise produces tachycardia. Chlorpromazine has a limited place in the premedication of children. Combined with other drugs it is useful for sedating infants for procedures not requiring general anaesthesia, for example for cardiac catheterization, removal of sutures or undertaking painful dressings.

The doses recommended (Smith and Rowe, 1958) are satisfactory, though not adequate for every patient: pethidine, 200 mg in 4 ml of solution, promethazine, 50 mg in 2 ml and chlorpromazine, 50 mg in 2 ml. One ml of this solution is to be given by intramuscular injection for every 9 kg (20 lb.) body weight. For large children the results are not as satisfactory as for infants under 11 kg (25 lb.).

(3) SEDATIVE, HYPNOTIC AND ANALGESIC DRUGS

Because the indications for sedation and the most effective methods of producing it are not the same for all ages, children can be divided into the following groups: (*a*) newborn; (*b*) three months to eighteen months; (*c*) eighteen months to five years and (*d*) five years and over.

Sedative drugs are given before operation to promote muscular and emotional relaxation by suppressing pain and diminishing apprehension. This helps to reduce the patient's metabolic rate upon which his oxygen requirements depend. In childhood the rate of metabolism is greater than in adult life. For this reason children, weight for weight, have a greater tolerance of all drugs, including anaesthetic agents, than do adults. This tolerance seems to reach its peak between five and eight years when the dosage requirements often approach that of the adult.

Sedation in relation to age.

(i) *Newborn.* For the newborn no sedative drugs are necessary before operation. The rate of metabolism at birth is low, apprehension is nonexistent and the reaction to painful stimuli seems to be comparatively unimportant in the first few weeks of life.

(ii) *Three months to eighteen months.* Sedatives given to young infants serve a useful purpose by reducing the metabolic rate and diminishing struggling during the induction of

anaesthesia. A smoother and safer anaesthetic is the result and it is easier to maintain anaesthesia without using explosive agents. This is particularly useful if the infant is chubby and the veins are difficult to find.

(iii) *Eighteen months to five years.* Children in this age group present the greatest problem in hospital. They are usually too young to understand the reason for the unwelcome experience. Because they are so emotionally vulnerable it is particularly desirable for them to reach the anaesthetic room fast asleep. Moreover veins suitable for the induction of anaesthesia are not always readily available. Under these conditions it is less traumatic to induce anaesthesia by inhalation techniques rather than to submit the child to numerous needle pricks.

(iv) *Over five years.* Although some children of five and six years and older are unduly depressed and apprehensive at hospital admission, most of them, when handled wisely, can be treated much as the adult when planning preoperative care and medication. This is particularly the case when veins are available for a quick induction of anaesthesia.

ROUTE OF ADMINISTRATION

In planning sedation for the child awaiting operation, the route of administration is no less important than the choice of the drug. The route of administration, while largely dependent on the age of the child, is determined too by the operation to be performed.

(a) *By mouth.*

Although this is often the simplest way of giving sedative drugs, the result, from the anaesthetist's point of view, is the least satisfactory. The rate of absorption from the stomach is very variable, particularly in children. The stomach contents may be undigested for many hours, so that the effect of any drug cannot be predicted with confidence. This delay in absorption may carry the risk of no sedation when it is most needed, and of delayed sedation when it is unwanted.

Drugs in capsules should never be given to premedicate young children, because absorption of their contents may be long delayed: moreover there is a risk of an undigested capsule being regurgitated and inhaled in the postoperative period.

In spite of the disadvantages offered by oral premedication, the method is comparatively safe and simple in practice, and sometimes it can be very satisfactory.

Drugs given by mouth to produce sedation.

Chloral. Chloral has a very unpleasant taste and produces effective sedation only when given in large dosage, namely 44 mg/kg (20 mg/lb.) body weight. Its particular value as a sedative before surgery is for infants who are to have an operation under local anaesthesia. It has been found unsatisfactory (by the author) as premedication before general anaesthesia; for under the large doses required to produce sedation, excessive secretions are frequently produced both during and following the operation.

Barbiturates. Drugs of this group are still the most highly favoured by anaesthetists for their narcotic effect. In spite of their many disadvantages, as yet they have not been surpassed by other drugs for oral premedication in children. Apart from the disadvantages common to all drugs given by mouth, barbiturates have unpleasant properties of their own. They have a very bitter taste, which sometimes makes it difficult to get the powder swallowed; and even if swallowed, it is sometimes returned. A palatable elixir is available, but the volume of fluid to produce sedation is too great to be safe in the pre-operative period. Furthermore, restlessness in the postoperative period is increased when barbiturates by mouth have been given as premedication. One explanation for this is that the barbiturates are not analgesic and may even be anti-analgesic (Clutton-Brock, 1960).

Phenothiazine derivatives. The sedation produced by trimeprazine tartrate is said to be as great as with the barbiturates; but the volume of fluid to be swallowed to produce sedation is large, which is a disadvantage in the pre-operative period. The sedation produced by promethazine, given alone, is not as great as with the barbiturates.

(b) *Rectal administration.*

The effect of sedatives given by rectum is also variable but far less so than when they are given by mouth. Rectal premedication is particularly

useful for children under the age of five years. A disadvantage is that some parents object to drugs being introduced into the rectum; and so do some children, but usually only the older ones, i.e. over six or seven years of age.

Another disadvantage of rectal premedication is that some of the drug may be returned; yet in spite of this, adequate sedation is frequently produced, particularly when the agent is quickly absorbed.

Choice of sedative for administration by rectum.

Barbiturates. Thiopentone is the barbiturate of choice for rectal administration. It can be given either in solution or in suppository form. The solution used is 5 per cent and the dose is 44 mg/kg (20 mg/lb.) body weight. Because only a comparatively small volume of fluid has to be injected, there is less risk of it being returned. Absorption is very rapid, sleep often being produced within seven or eight minutes and the maximum effect is reached after half an hour. Failure to produce sedation is rare. The main disadvantage is that the depth of sleep may be profound and is often associated with respiratory depression. It is therefore *essential* that once the drug has been given the patient must have the *constant* supervision of a trained nurse or anaesthetist. This contra-indicates its use in a busy centre where trained nurses are scarce. Recently trial has been made of thiopentone in suppository form, supplied in 125 mg, 250 mg, and 500 mg sizes. Preliminary results have been successful. Sleep is produced on a dosage of 33 mg/kg (15 mg/lb.) body weight, and although the action is almost as rapid as with the solution, the danger of such deep narcosis is not apparent. The effect of the thiopentone suppository starts to wear off within one hour of administration. These suppositories, in a dosage of 22 mg/kg (10 mg/lb.) have been used with success for cardiac catheterization when the "lytic cocktail" has not been adequate. In even smaller dosage they have proved useful for maintaining anaesthesia and promoting vasodilatation during prolonged hypothermia. Quinalbarbitone sodium and pentobarbitone sodium can also be given by rectum, either in solution or suppository form. These should be administered at least one hour before operation. The effect is less reliable than with thiopentone but the advantage they offer is that the narcosis produced is not as deep as that produced with thiopentone.

Tribromoethanol. This has nothing to commend it, for it has no advantages over thiopentone. The solution is unstable and needs careful preparation.

Paraldehyde. This is the safest basal narcotic. In therapeutic doses it does not depress respiration nor produce undesirable cardiovascular changes. However, it has certain disadvantages. It requires considerable dilution when given by rectum, so that a large volume of fluid must be retained to produce the desired effect. The maximum effect is not reached for an hour or more. Excretion is so delayed that postoperative narcosis may persist for several hours. Finally, the odour of paraldehyde is particularly unpleasant.

(c) *Drugs given by injection.*

This method of administration is the mainstay of premedication for children over five or six years of age as it is for adults.

Opiates. Morphine or papaveretum in combination with hyoscine or atropine are drugs well suited for the premedication of children over 15.9 kg (35 lb.) body weight (about five years of age). Children—on the recommended dosage—are usually drowsy but co-operative on reaching the anaesthetic room. As they usually have veins available for the induction of anaesthesia they are not likely to have unpleasant memories of the anaesthetic. In contrast younger children are less fortunate. Because they tend to suffer emotionally from hospital admission they particularly need good pre-operative sedation. But frequently sedation is inadequate when papaveretum and hyoscine are given in this age group according to the scale of dosage related to body weight. Increasing the dose carries the risk of serious respiratory depression. It is therefore safer and preferable to premedicate by some other route (rectal or oral), anaesthesia being induced thereafter by the inhalation of gases.

The dose of papaveretum for premedication is 0.6 mg/kg (0.29 mg/lb.) of body weight. This is used for all age groups, and is a slight increase for the smaller children than that originally recommended by the author (Anderson, 1951).

When the tolerance of smaller children to papaveretum was found to be high, it soon became apparent that this age group needed as much as, indeed even more than, the older children, to produce adequate sedation.

In order to secure accurate dosage of opiates, particularly when the dose is small, it is imperative to use a dilute solution. The prescription should always state the weight of drug required.

Pethidine. Pethidine is a very satisfactory substitute for the opiates, as in adults. The dose is 1.1–2.2 mg/kg (0.5–1 mg/lb.).

Contra-indications to premedication with the opiates, or pethidine combined with hyoscine, are determined by the type of surgery, and the method proposed for the maintenance of anaesthesia and the age of the patient. Thus heavy sedation using the opiates is not successful when followed by an "open" method of anaesthesia such as the oral insufflation of oxygen and ether for tonsillectomy. The depression of respiration produced may make it very difficult to maintain a level of anaesthesia deep enough to meet the surgeon's requirements: while the recovery time will be prolonged due to delayed excretion of the ether.

TIME OF ADMINISTRATION OF PREMEDICATION

(See Table I)

The choice of time of administration of drugs used for premedication is as important as the choice of the drug and the route. The aim should be to have the maximum sedative effect at the time of induction of anaesthesia If given too late, a wakeful, frightened child may arrive in the anaesthetic room, and the narcotic action of the drug will be delayed until the operation is in progress, or in a short procedure after it is completed. It is better not to give a sedative at all if it cannot be given at the correct time. If the belladonna drugs are given too late or too early, excessive mucus secretion will prove troublesome and dangerous.

TABLE I

Time interval between administration of premedication and the induction of anaesthesia.

Route	Time interval before induction of anaesthesia
By mouth:	
Chloral	45 minutes
Barbiturates, Phenothiazine drugs	90 minutes
By rectum:	
Thiopentone	30 minutes
Tribromethanol	30 minutes
Paraldehyde	60 minutes
Pentobarbitone, Quinalbarbitone	60 to 90 minutes
By injection:	
Atropine	30 to 40 minutes
Opiates, Pethidine, Phenothiazine drugs, Hyoscine	60 to 90 minutes
Lytic "cocktail"	45 to 60 minutes

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PAEDIATRIC ANAESTHESIA

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THE CHILD AS A SUBJECT FOR ANAESTHESIA

Discussion of paediatric anaesthesia is made difficult because the patient is undergoing continuous development and there is no point at which the child becomes an adult. It is therefore profitable to consider the differences between the youngest infant and the adult which may influence the response to anaesthesia, and to regard children in intermediate age groups as occupying some intermediate position as subjects for anaesthesia. Such an approach to paediatric anaesthesia is not without its problems, for there are certain characteristics which influence the anaesthetic problems of the premature infant, which are absent at full term; thus even the time of birth is to be regarded as a somewhat arbitrary point on the scale of development. In addition there are certain responses to anaesthesia which differ from the adult pattern in one direction at one stage of development, and in a different direction at another stage An instance of this is the effect of certain anaesthetic techniques on the heat conservation of the child. Under the age of about six months anaesthetized infants tend to become hypothermic; above this age there is a tendency towards hyperthermia, both of which responses differ from the adult, but in different directions.

In spite of difficulties in the concept of progressive change from the newly born to the adult state, it is advantageous to consider the neonate in some detail, to regard the change to the adult as progressive, and to note those changes which do not occur in a linear fashion with increasing age.

Differences between the child at birth and the adult of interest to the anaesthetist may be considered systematically.

The endocrine system.

The infant at birth is generally regarded as a good operative "risk" but during the early days of life tolerance to trauma is rapidly diminished. In more recent times it has become evident that tolerance is related to the ability of the adrenal cortex to respond adequately to the stress imposed —a response which may be measured in terms of the changes induced in electrolyte metabolism.

A part of the pattern of this change in adults is indicated by postoperative balance studies (Moore and Ball, 1952) which reveal a loss of nitrogen and potassium. If the ratio of potassium loss to nitrogen loss (K/N ratio) is measured, it is found to be higher than that of normal cells. That is, the K/N ratio is what it would be if there were a breakdown of cells liberating nitrogenous products and potassium, and in addition a loss of intracellular potassium from cells which also lose their nitrogenous content. Rickham (1957) has demonstrated that the newly born infant also shows a negative nitrogen and potassium balance postoperatively; in this case the K/N ratio is that of normal cells, which suggests that cells break down and liberate their nitrogen and potassium, but, as opposed to the adult response, potassium is not lost by cells which do not also lose their nitrogenous content.

Rickham's work suggests that this neonatal pattern of adrenocortical response changes to the adult pattern quite early in life, i.e. at the age of three or four weeks, but further research is necessary.

These metabolic responses to surgery and the long accepted belief that the operative risk increases during the first weeks of postnatal life, must be considered in relation to the known facts concerning adrenocortical function in pregnant women and in newly born infants. During pregnancy there is a progressive rise in the maternal blood level of corticosteroid compounds which reaches a peak during labour, and at this time the foetal cord blood levels parallel the maternal blood levels. After birth there is a fall of corticosteroids to a very low level. Further-

more, although the adrenal of the infant is of considerable size, its cortical cellular organization is not that of a normally functioning adult adrenal cortex, and is of little functional value. The infant at birth, then, has had available—until the placental circulation ceases—an exogenous supply of cortical hormones, which ultimately give rise to very high blood levels. At the time of birth this source of supply is withdrawn. This may account for the diminishing tolerance to surgical trauma in the day following birth, and for the failure of the infant to show the normal adult pattern of metabolic response to trauma.

Experience suggests that in later childhood adrenocortical depletion as a result of accident or operative trauma or of acute disease, is not uncommon (Rees, 1959), and that in children aged up to 10 years, failure of resuscitation despite adequate blood flow, and electrolyte replacement is frequently overcome by substitution therapy. The introduction of rapidly acting intravenous preparations of hydrocortisone has made assessment of adrenocortical function by therapeutic test a rapid and easy procedure. The author has been impressed in cases of massive surgery for malignant conditions in childhood by the effect of supplementary cortisone therapy (1.5 mg/kg per diem) on the postoperative course.

The blood.

The haemoglobin value of the blood of the infant at birth is higher than that of the adult, and the difference is more marked in the premature than in the full term infant, where it often exceeds 150 per cent (Sahli*). During the early months of life the haemoglobin falls to a value of 75 per cent at 3 months, and thereafter rises throughout infancy and childhood to the normal adult value at about 12 years. The necessity to appreciate these variations in haemoglobin value is obvious, for attempts to "correct" them might be disastrous, and failure to consider them might lead to an erroneous assessment of fitness for operation. The high haemoglobin values at birth should not be a deterrent to the replacement of blood loss.

In addition to the difference in the amount of haemoglobin between the blood of adults and infants there is also a qualitative difference in the haemoglobin. At birth there is a considerable proportion of foetal haemoglobin in the blood, that is, of a haemoglobin compound whose oxygen dissociation curve lies to the left of that of adult haemoglobin. This is destroyed in the early days of life, and its breakdown is responsible for the appearance of the physiological jaundice of the newborn.

The blood volume of infants expressed as a function of weight is slightly higher than that of the adult, and is about 84 ml/kg. The normal full term infant, therefore, as a blood volume in the region of 300 ml, and small losses may be a considerable proportion of the total. Accurate assessment and replacement of blood in these circumstances is essential.

The respiratory system.

The respiratory physiology of the infant has been described in some detail elsewhere in this issue (see page 97). Respiratory differences between the infant and the adult of importance when considering the infant as a subject for anaesthesia are:

(*a*) The fatigability of the chemical control mechanisms of ventilation, i.e. the failure to maintain the ventilation response to decreases in the oxygen percentage and increases in the carbon dioxide percentage of the inspired gases.

(*b*) The way in which the minute volume is achieved by relatively high respiratory rates and relatively low tidal volumes.

As a result of (*b*), increases in the deadspace (e.g. in inhalation apparatus) proportional to the minute volume will have a greater effect on the effective ventilation in the infant than in the adult. As a result of (*a*), the infant is unable to compensate except for brief periods.

The newly born infant frequently shows a periodic type of respiration, such as is seen in adults, when the primary driving force of the respiratory neuromechanism is a falling oxygen tension rather than a rising carbon dioxide tension (e.g. at high altitudes).

A regular rhythm may be established by providing an oxygen enriched inspiratory mixture. Howard and Bauer (1949) suggest that the origin of the periodic breathing of the infant is similar to that in the adult. That this is probably the case is further suggested by the fact that the carbon dioxide tension is lower in infants than in adults. This dependence on a failing oxygen

* 100 per cent = 14.99 mg./100 ml.

tension for respiratory stimulation may be the result of a diffusion defect due to the small respiratory surface of the infants' lung described by Engel (1947). Studies show that the diffusion capacity in relation to size is constant in all age groups, but further work is necessary to elucidate the relationship between diffusion capacity and oxygen requirement in infancy.

The apparent deficiency of the infant's respiratory system may be overcome during anaesthesia by control of the respiratory movements which ensures (*a*) that ventilation is adequate—despite the inability of the centre to maintain a normal ventilation response—and (*b*) a reduction of the metabolic demands of the body by providing the energy for pulmonary ventilation from an external source (see also section on temperature control).

Cardiovascular system.

Up to the time of birth the heart has had to provide a circulation through both the body tissues and the placental mass. The additional load is, by virtue of the foetal communication between the pulmonary and systemic circulations, shared between the right and left ventricles. As a result, at birth the development of the two ventricles is approximately equal, that is, their wall thickness is similar, and the neonatal e.c.g. shows a pattern which would, in an older patient, be interpreted as indicating right ventricular hypertrophy. As a natural sequence of this state the pulmonary arterial and aortic pressures are very similar, and the normal adult differentiation between these two pressures develops in the early months of life. Also up to the time of birth the infant has had no negative intrathoracic pressure to assist the venous return (his fluid environment possibly makes this less necessary).

The infant at birth tolerates positive pressure ventilation well, in that reduction in blood pressure with this form of ventilation is much rarer than in adults. The high pulmonary artery pressure and the independance of a *negative* intrathoracic pressure for cardiac filling might well be expected to produce such a picture.

Anatomy of larynx and bronchial tree.

The larynx of the newly born infant differs somewhat from that of the adult in that:

(i) The neonatal larynx is higher in relation to the cervical vertebrae; the cervical cartilage at birth is opposite the 4th cervical vertebra, as compared with the 7th cervical vertebra in the adult.

(ii) The epiglottis is curved from side to side and is not, as in the adult, a flat, spade-like structure.

(iii) The narrowest part of the larynx is at the cricoid ring, and not at the level of the chords as in the adult.

(iv) The long axis of the larynx is directed *forwards and downwards* rather than downwards, as in the adult, and the thyroid cartilage is much more closely attached to the hyoid bone than in later life.

The practical effect of these anatomical differences is that (1) a laryngoscope blade which passes posterior to the epiglottis is more suitable than one of the Macintosh type for the smaller infants, as it is not possible with the latter to flatten out the curvature of the epiglottis; and (2) in order to line up the larynx with the laryngoscope blade it is necessary to depress the larynx with a finger on the neck during intubation. Details of intubation techniques are described in the section on intubation.

Heat regulation in infancy and childhood.

It is well known that trivial causes will produce marked variations in the temperature of infants, e.g. teething is often accompanied by pyrexia. During and after anaesthesia the variations in temperature may be gross.

Children used frequently to have a progressively rising temperature postoperatively, often terminating in convulsions and death. Various factors contributed to the development of this state; they were: (1) ether anaesthesia; (2) carbon dioxide retention; (3) respiratory obstruction; (4) atropine premedication; (5) dehydration; (6) high environmental temperatures and (7) heavy drapes.

The last four of these may be termed non-specific contributing factors, in that they could accentuate a pyrexia due to any cause, whether related to anaesthesia or not. The first three may be termed specific factors related to anaesthesia; the common feature being that they all tend to increase the work of respira-

tion. That an increase in the work of respiration produces pyrexia in children is demonstrated by the effect of abolishing the hyperpnoea of salicylate poisoning with relaxant drugs, or by relieving respiratory obstruction in acute respiratory disease in children by tracheo-bronchial toilet. In each of these cases pyrexia is rapidly reduced.

Similarly, if the work of respiration is abolished during anaesthesia by using controlled ventilation, the temperature of the child tends to fall, and this is repeatedly observed even when the "non-specific" factors are present. It is worth noting that the condition of postoperative hyperthermia was first described by Ombredonne, and also that Ombredonne's inhaler is illustrated in one text book as an example of inhalation apparatus in which little effort has been taken to mimimize deadspace and resistance to aspiration, the two factors which are likely to increase respiratory work (Macintosh and Mushin, 1957).

Hyperthermia is a hazard only in children above the age of six months, below that age there is a tendency for the child to lose heat during anaesthesia. Ordinarily a fall in temperature would be regarded as innocuous in an anaesthetized patient. There is, however, a disease which develops in newly born infants termed sclerema, which is more common in premature than in full term infants, and in it there is an alteration in the physical properties of the subcutaneous tissues, which acquire a hard marble-like appearance. Sclerema appears to be in some instances the result of hypothermia (Bower et al., 1960), although it is more common in infants who have undergone surgery than in premature infants who have been hypothermic but have not been subjected to surgery. The chemical nature of the tissue change is not known, and there is need for research into this and into the relationship between the condition and hypothermia. It may well be that the primary cause is a reduction in the skin circulation, which may be brought about by a variety of causes, including surgery, blood loss, "stress", and hypothermia. Most authorities believe at the present time that in the neonatal infant it is wise to limit the fall in temperature during anaesthesia by insulation and by the application of heat. For this purpose a water mattress is preferable to an electric pad.

Response to relaxant drugs.

The response of the child to relaxant drugs is essentially similar to that of the adult. The sensitivity of the child to suxamethonium is rather less than that of the adult. This difference is particularly great in the newly born infant, falls sharply during the early weeks of life and then progressively throughout childhood (Telford and Keats, 1957). There appears also to be a reduced sensitivity to tubocurarine in childhood after the neonatal period.

In the neonatal period the infant shows a marked sensitivity to tubocurarine and a marked resistance to suxamethonium. This type of response to relaxant drugs is essentially similar to that of the myasthenic patient. There are other similarities, in that the infant never exhibits muscular fasciculation following the injection of suxamethonium and that he tends to develop rapidly a "dual response".

INHALATION APPARATUS FOR CHILDREN

Any discussion on inhalation apparatus must start with a consideration of the relative virtues of closed and open circuits for children in the various age groups. The closed circuit with carbon dioxide absorption has been modified, and miniaturized for application to the smallest infants both in the form of circle and "to and fro" absorbers. Before discussing the merits of these systems for infants, it is well to remind ourselves of the reasons for their use in adults. The carbon dioxide absorber was introduced into anaesthetic practice at the same time as cyclopropane because the cost of this gas would have been prohibitive without closed circuit anaesthesia. To this day, economy of anaesthetic gases must be regarded as the prime factor influencing our use of the carbon dioxide absorber. This method of administering gases has other less definite points in its favour; these are that: (*a*) water vapour is conserved and humidified gases are inhaled, (*b*) heat is conserved, (*c*) controlled ventilation is more readily performed and (*d*) the explosion hazard is less.

In the smallest patients, whose normal minute volume may be in the order of 500 ml/min, it would seem that economy of gases could scarcely be considered as a reason for choosing a closed circuit in preference to some non-rebreath-

ing arrangement or a semi-open circuit. The conservation of water vapour may, if considered desirable, readily be accomplished by humidifying the anaesthetic gases prior to their entry into some open or semi-open circuit; the conservation of heat is of doubtful advantage in children —except possibly in the newly born. Thus the advantages of a closed circuit arrangement in the infant are doubtful, whereas the disadvantages of more cumbersome apparatus, and an inevitably greater deadspace and resistance to respiration are real. Therefore there appears to be little place for the carbon dioxide absorber for anaesthesia in infants and young children.

The alternatives to closed circuit apparatus for the younger infants (when endotracheal anaesthesia is employed) are; (1) paired non-rebreathing valves and (2) T-piece arrangements.

The employment of an expiratory valve near the patient and an inspiratory valve to prevent the patient from expiring into the apparatus is as old as anaesthesia itself. A compact unit with minimal deadspace to contain the two valves, was first constructed by Leigh (Leigh and Belton, 1949); this was later modified by Slater and Stevens (1951) with a similar valve mechanism. The deadspace of these valves is far from negligible when considered in relation to the tidal volumes of the smallest infants. A disadvantage is that the anaesthetist has to occlude the expiratory valve with a finger if positive pressure breathing is to be employed; this necessitates access to the patient's face. The Fink valve (Fink, 1954) incorporates a mechanism which closes the expiratory valve if the pressure in the reservoir bag is raised, and allows it to open if the pressure is released, thus permitting controlled ventilation to be carried out without manual operation of the expiratory valve. An important danger associated with the use of this principle is that if the reservoir bag becomes distended (e.g. by the inadvertent use of the oxygen by-pass valve), the rise in pressure within the bag will close the expiratory valve, and the controlled flow of gas from the anaesthetic machine will produce a large increase of pressure within the reservoir.

Paired non-rebreathing valves have found little favour for paediatric anaesthesia in Britain; the alternative which is widely used is the Ayre's T-piece (or some modification of this arrangement). The special virtues of this apparatus are that (*a*) it is compact and (*b*) the deadspace is minimal. The disadvantage is that it is extremely uneconomical as regards the ratio of fresh gas flow to minute volume required to eliminate rebreathing. This ratio has been calculated by Mapleson (1954) and determined experimentally by Inkster (1956) using a mechanized model lung to simulate respiration. Conclusions reached by both these workers suggest that if the input of fresh gas is in the order of twice the estimated minute volume of the patient, then rebreathing is not significant. As flow rates of gas up to about 8 l./min are quite manageable and as the normal minute volume rises to about 4 l./min at 10 years, one may regard the T-piece as suitable for children up to that age. The length of the open tube of the T-piece does not affect rebreathing in the system provided the flow rate of fresh gas exceeds the minimum requirement. The T-piece system may be adapted for controlled ventilation by fitting to the open end of the expiratory limb a 500 ml bag which has an open-tail. By manual compression of the bag with the open end partly occluded it is possible to vary the pressure in the exhaust limb of the T-piece, and thus perform intermittent positive pressure breathing.

In discussing manual controlled ventilation with small capacity bags, it is necessary to emphasize that for any given degree of muscular effort on the part of the anaesthetist, the pressure developed within the bag varies inversely with its diameter.* Unless this is appreciated the anaesthetist will ventilate at much higher pressures when he comes to use a small bag.

INDUCTION OF ANAESTHESIA IN CHILDREN

The induction of anaesthesia in children may be

* The physical law which relates the pressure difference on the two sides of a spherical membrane inversely to the radius of the sphere, accounts for the higher pressure developed in the small bag, for the anaesthetist by his efforts produces tension in the membranes of which the bag is made, and the tension in the spherical membrane produces a pressure difference between the inside and the outside of the bag. The same physical laws enable the neonate, with a diaphragmatic arch of small radius, to produce a negative intrathoracic pressure comparable to that which the adult can produce despite the thinness of his diaphragmatic muscle.

by inhalation or by the intravenous route. Many workers have designed teddy bears with cunningly concealed tubes which allow them to belch forth cyclopropane and other unpleasant vapours. Such arrangements are to be condemned both on psychological and physical grounds, for they are deceptions. They necessarily have a narrow orifice from which the gases issue, whereas to "drift" heavy gases on to the child's face it is most effective to have a wide orifice through which the velocity will be less.

Nisbet and Wilson (1959) have described a method of inducing anaesthesia in children with nitrous oxide, oxygen and ether in which a high concentration of ether vapour is delivered from a face piece held some distance above the face; the mask is lowered slowly as induction proceeds. This appears to be a method readily employed by the inexperienced.

The kindest method of inducing anaesthesia in children is by the intravenous route (Rees, 1950; Hamer Hodges, 1959). By using fine needles (26 S.W.G.) venipuncture is virtually painless. As children are subjected to innumerable injections, both for immunization purposes before admission to hospital, and after admission, it is helpful if the anaesthetist warns the child that the injection will not be the same as those used previously in the ward. The expression a "scratch" is preferable to a "prick". Using fine needles and distracting the child in some way at the moment of pricking the skin, causes him to be frequently unaware of the venipuncture.

If induction is to be followed by intubation the intravenous injection permits the introduction of a relaxant through the same needle.

The sites of choice for intravenous injection vary with the age of the child. Until the growth of hair prevents it, the scalp veins provide the easiest site in infants; the volar aspect of the wrist is preferable between the ages of 6 months and two years. Thereafter the dorsum of the hand and the anticubital fossa have veins which are easily entered with a needle.

The prime advantage of the intravenous route in infants and children is that it allows a pleasant induction without resort to excessively heavy premedication. What might be regarded as a disadvantage is the marked tendency of children to develop laryngeal spasm when inhalation agents are introduced following thiopentone. If, however, the technique adopted involves intubation, this difficulty is overcome and intubation offers other special advantages in children.

INTUBATION IN NEONATES

The technical difficulties of intubating the smallest infants make it unwise to induce apnoea with intravenous drugs prior to intubation, and in the younger infant an inhalation induction may be difficult, prolonged, and fraught with the risk of regurgitation and aspiration. Most authorities, therefore, intubate these infants before the induction of anaesthesia. The age up to which this practice should be used is debatable; the author holds that after four weeks more orthodox methods should be used; others carry out this manoeuvre in older infants. Clearly the laying down of an arbitrary age beyond which it should not be used is useless in view of the varying state of development of different infants at birth, and of their subsequent variable rate of development.

INTUBATION IN CHILDREN

Intubation of children used to be regarded as a procedure carrying a high incidence of major complications and it has been suggested that it should be avoided if possible. Present experience indicates that the hazards have been overrated (in the hospitals in which the author serves, over 35,000 intubations of children in the last five years have produced major complications in only one patient—see later). It is profitable to consider the difference in the present conditions from those which existed when the myth of dangers from intubating children arose; the following factors possibly account for them:

(1) Twenty years ago opiates were regarded as contraindicated in children, who were commonly premedicated with atropine alone, and subsequently anaesthetized with ether—a combination which leads to irregular respiration with considerable tracheal tug persisting throughout operation; this process of relative movement between the larynx and tube would be likely to traumatize the larynx.

(2) It is only in recent years that the dangers of infusing infants with normal saline solutions

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has been appreciated. The empirical infusion of large quantities of such solution was often carried out for the correction of dehydration; a procedure which we now know frequently gives rise to generalized oedema. That laryngeal oedema may occur as part of a generalized oedema was demonstrated to the author by a patient with burns, requiring intubation and resuscitation for twenty-four hours, during which time the child developed generalized oedema from unrecognized anuria, and following extubation, laryngeal oedema.

(3) Endotracheal tubes have improved in quality over the years, and chemical methods of sterilizing them have been abandoned.

The anatomy of the infant larynx has already been described as has the necessity for a straight laryngoscope in the younger age groups. In the newly born the anterior tilting of the larynx makes visualization more difficult than in the older child or the adult—a difficulty which is easily overcome by having an assistant press the larynx gently backwards with a finger on the neck during laryngoscopy. Because of the position of the larynx in early infancy, the tip of the laryngoscope blade frequently passes down the pharynx beyond the epiglottis without the latter being seen. This is especially liable to happen in the premature infant; some anaesthetists therefore prefer, in the smaller infants, deliberately to pass the instrument deep into the pharynx and to explore the anterior wall for the larynx as it is withdrawn. During this phase of the manoeuvre the tongue is pulled upwards by the instrument instead of being pushed downwards as in the introduction phase.

Older children present no special technical difficulties in the absence of anatomical abnormalities.

Anatomical abnormalities affecting intubation.

Accentuation of the forward angulation of the larynx in the premature infant has already been mentioned, and occasionally the larynx appears to be overhung by the base of the tongue which bulges backwards over the larynx. This state may persist abnormally late in development and up to the first year or two of life. It is present when the lower jaw is not fully developed as in premature infants and when mandibular development is delayed—a condition termed micrognathia. Micrognathia occurs in association with an incomplete cleft palate and respiratory obstruction caused by the tongue being held—by virtue of a small mandible—in proximity with the posterior wall of the pharynx (glossoptosis); this combination is termed the Pierre-Robin Syndrome. This syndrome gives rise to very difficult conditions for intubation, which will be necessary for the repair of the cleft palate. One authority describes a patient in whom intubation proved impossible, and surgery had to be delayed (Smith, 1959). The author has on occasions spent upwards of thirty minutes intubating such a child. Grave degrees of the condition are fortunately rare but a high proportion of infants anaesthetized for the repair of a posterior cleft palate are relatively difficult to intubate as compared with normal children. (N.B. This condition is associated with an incomplete cleft palate, and not with total cleft palate and lip.)

Subglottic stenosis.

Stenosis of the larynx at the level of the cricoid ring is occasionally met with incidentally in children. It may not be so gross as to produce stridor but is sufficient to allow the passage of a very small endotracheal tube.

MAINTENANCE OF ANAESTHESIA IN CHILDREN

The respiratory deficiencies of the infant during early life and the hazard of hyperthermia in older children suggest that controlled ventilation during the maintenance of anaesthesia has special advantages. It should be regarded as an essential part of the technique for prolonged operations, and is highly desirable for shorter procedures. Anaesthesia can be maintained at very light levels with nitrous oxide-oxygen and a relaxant drug, with the result that recovery is rapid. The advantages of nitrous oxide as the sole anaesthetic agent in children are the same as those for adults. In addition there is an advantage peculiar to paediatric practice, e.g. if anaesthesia is induced with thiopentone in children and they are intubated with a short acting relaxant and permitted to breathe spontaneously on one of the more potent inhalation agents, there is a high incidence of extubation laryngeal spasm, which may be so persistent as to become alarming:

maintenance of anaesthesia or controlled ventilation with a relaxant and nitrous oxide completely eliminates this complication. The phenomenon is difficult to explain.

If induction is by the intravenous route—the advantages of which have already been described—the change to an inhalation agent is slow and often accompanied by laryngeal spasm. If induction precedes intubation using a short acting relaxant drug, and anaesthesia is maintained with an inhalation agent and if spontaneous respiration is allowed; then extubation on spasm is common. There are, therefore, cogent practical and theoretical reasons for maintaining anaesthesia with controlled ventilation, a relaxant drug, nitrous oxide and oxygen.

ESTIMATION OF BLOOD LOSS

Estimation of blood loss during surgery on an infant weighing, e.g. 7 lb. (3.1 kg), with a blood volume of the order of 350 ml must be carried out to a high degree of accuracy if replacement is to be reasonably satisfactory. There are three commonly used methods for determining blood loss; by swab weight, by extraction and measurement of electrolytes, and by extraction and measurement of haemoglobin.

Weighing the swabs. The customary method of assessing the weight of a number of dry swabs and subtracting this from the weight of the used swabs is not sufficiently refined for paediatric surgery. If swab weight is to be used as an index of blood loss then each of the swabs must be weighed before and after use. This method precludes the use of wet swabs, does not take account of evaporation losses, or of losses apart from the swabs.

Electrolyte measurement. The change in electrical conductivity of a known volume of water after all swabs and other blood-stained materials have been washed in it is sometimes used as an index of blood loss—the disadvantage of this method is that all body fluids are measured as blood—this is somewhat confusing in, e.g., cardiac surgery when a patient in failure may have pleural and pericardial effusions, or in abdominal or genito-urinary surgery.

Haemoglobin measurement. The third method is to extract haemoglobin from the soaked theatre linen in a known volume of water, and to estimate the concentration of haemoglobin by orthodox means; this is a satisfactory, practical and reasonably accurate method for determining small blood losses.

POSTOPERATIVE PULMONARY COMPLICATIONS IN INFANCY

The infant depends to a much greater extent than the adult on diaphragmatic movement for ventilation exchange. This is the inevitable result of the configuration of the thoracic cage in which the angle of the thoracic inlet, and the ribs, are much more horizontal than in the adult, and therefore are less well able to contribute by their movement to the increase in thoracic volume during inspiration. As a result of the ineffective rib movement upper lobe ventilation is more liable to suffer in circumstances giving rise to respiratory embarrassment than lower lobe ventilation, and thus, in the younger children, postoperative pulmonary collapse is more prone to occur in the upper lobes. It is better, therefore, to nurse such children postoperatively with a head-up tilt, and in view of the tendency of pulmonary collapse to develop, they should be treated in an atmosphere of high humidity, either an incubator, or in "cold-steam". The patient should be nursed in the lateral position, and turned from side to side frequently.

In spite of these measures it is not uncommon for pulmonary complications to occur, either as a result of regurgitation and aspiration, or immobility. In such patients tracheobronchial toilet is necessary, which may be carried out by intubation, and the passage of a catheter through the endotracheal tube, or by bronchoscopy. It was stated by Adriani and Gregg (1954) that the angle between the trachea and the main bronchi is equal on the two sides in infancy. This statement has persisted in the anaesthetic literature; it does not occur in the literature of other specialties (for instance, radiology), and can be demonstrated to be untrue during bronchoscopy. A catheter passed down an endotracheal tube tends to pass into the right main bronchus in the infant as in the adult, and it may therefore be necessary to resort to bronchoscopy for effective tracheobronchial toilet on the left side.

SUMMARY

The way in which the physiological make-up of the infant differs from the adult in so far as it affects him as a subject for anaesthesia is described. The suitability, in view of these differences, of techniques involving controlled ventilation for children is emphasized, and the factors which have made anaesthetists reluctant to use endotracheal intubation, an essential part of such a technique, are discussed.

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CORRESPONDENCE

REBREATHING IN AYRE'S T-PIECE

Sir,—On behalf of Dr. Simpson and myself I should like to apologize to Professor Mushin for the fact that Dr. Mapleson was not quoted in our paper "A Restatement of Anaesthetic Principles" (*Brit. J. Anaesth.*, **31**, 464). We were, of course, familiar with the work of Dr. Mapleson (1954, 1958) and also of the many other authors who have discussed Ayre's T-piece, but our article was concerned with principles rather than details. A meticulous justification of every statement would have made the article inordinately long, and there would have been an almost unlimited list of references.

In view of Professor Mushin's comment, it would seem that a full justification of the remark made by Dr. Simpson and myself about the T-piece might not be out of place, and a more extended communication will be devoted to this. For the moment I should merely like to say that we do not regard Dr. Mapleson's calculations as being the whole answer to the clinical use of the T-piece; we rather incline to agree with Davies, Verner and Bracken (1956) who, quoting Mapleson and others, stated: "From their publications it can be seen that there is no general agreement either on the minimum flow rate necessary or on the most effective semi-closed system."

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THE EVOLUTION OF ANAESTHESIA

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CHLOROFORM

CHLOROFORM was discovered in 1831 independently by three chemists.. Priority is usually awarded to Samuel Guthrie (1782–1848) of Sackets Harbor, New York, who published an account in *The American Journal of Science and Arts*, in October, 1831. It appears (Pawling, *Dr. Samuel Guthrie*, Brewster Press, 1947) that the discovery was made in February of that year, and the article was submitted for publication in July. Eugène Soubeiran (1793–1858), the second independent discoverer, claimed priority for his paper, in the *Annals de Chemin et de Physique*, for October 1831, but, owing to the second French Revolution, the issue was delayed until the beginning of 1832. The third discoverer, Justus von Liebig (1803–1873), published a note in the *Annalen der Physik* in November 1831. Of the three discoverers, Guthrie was the only one who used the modern method of manufacturing chloroform from alcohol and bleaching powder. He advocated his product, which he believed to be a form of "chloric ether" as an intoxicating beverage, and it came to be known as "Guthrie's Sweet Whiskey". Chloric ether, otherwise known as Dutch Oil or Liquid of the Dutch Chemists, had been known since 1796: its composition is uncertain, but it was probably an unstable mixture of chlorinated hydrocarbons. Soubeiran gave the name "bichloric ether" to the substance which he produced and which he believed to have the formula CHCl; von Liebig called his preparation "chloride of carbon" and assessed its formula as C_4Cl_5.

The formula of chloroform was worked out by Jean-Baptiste Dumas in 1834. Ignorance at that time of the bi-atomic nature of the hydrogen molecule led him to express it as C_2HCl_3 and he bestowed upon it its name, thinking it to be a halogen derivative of the imaginary radical "formyl".

Chloroform was quickly introduced into medicine and became a standard constituent of the "cough-bottle". As early as 1831, Ives of New Haven used chloroform vapour for the treatment of a patient with dyspnoea, but this seems to have been an isolated event. The liquid was recommended for such diverse conditions as hysteria, neuralgia and cancer during the twelve years after its discovery.

In 1842, R. M. Glover, of Newcastle upon Tyne, injected various brominated and chlorinated compounds into the veins and arteries of dogs and rabbits. He noticed that chloroform produced coma, a lowering of the blood pressure, and irregularity of the action of the heart (*Edinburgh Medical Journal*, 1842, **58**, 353).

Animal experiments with chloroform were also carried out by M. J. P. Fluorens (1794–1867) during February and March 1847; he recognized the anaesthetic action of the drug, but considered it too toxic for clinical use.

The story of the introduction of chloroform anaesthesia has often been told. It was a chemist, David Walde of Liverpool, who had had much to do with the preparation of pure specimens of this substance, who first recommended its use as an anaesthetic to Professor (later Sir) James Young Simpson. The latter had introduced anaesthesia with ether into the practice of midwifery on January 19, 1847, but he was not altogether satisfied with this substance, particularly because of the objectionable smell which hung about his clothes after its administration. After meeting Waldie in October 1847, Simpson procured a specimen of chloroform from Messrs. Duncan, Flockhart & Co., and his assistant, Matthews

Duncan, ascertained its narcotic properties by inhalation in the first day or two of November. On November 4, Professor Simpson, Drs. Keith and Duncan had dinner at Simpson's house, 32 Queen Street, Edinburgh, and after the meal they inhaled chloroform from tumblers, with devastating results. Unfortunately the date of the first administration of chloroform it not known, but, by November 8, it had already been used in midwifery and for several minor operations. Simpson's paper, *Account of a New Anaesthetic Agent as a Substitute for Sulphuric Ether in Surgery and Midwifery*, was read to the Medico-Chirurgical Society of Edinburgh, on November 10, and appeared in print on November 15; it was subsequently reprinted, with some additions, on numerous occasions.

The use of chloroform quickly spread to England: on November 20, "several operations were performed at St. Bartholomew's Hospital, upon patients rendered insensible to pain by the administration of chloroform. . . . The chloroform was administered by Mr. Tracey, by means of a thick flat piece of sponge. . . ." (*Lancet*, 1847, **2**, 571). Within a short time, ether had been displaced from its position and chloroform had become the routine anaesthetic in Britain and elsewhere, although the former still retained its popularity in the Northern States of the U.S.A. Familiarity, of course, bred contempt, and, on January 28, 1848, the first death occurred during the inhalation of chloroform. This case was reported very extensively in the medical press of the time: it is surprising that it should have made such a stir, for there had already been at least three deaths during the inhalation of ether, one in France, one in Russia, and one in Alabama, but these had all received but scant notice. The deciding factor, was, probably, the fact that the victim of chloroform was a young, healthy girl undergoing a very trivial operation, an operation moreover which she had undergone safely a fortnight before under the influence of ether. Professor Simpson plunged into print in defence of chloroform, denying that it could have been the anaesthetic which had caused death, and asserting that this had been the result of the efforts at resuscitation undertaken by the two doctors present: they had poured brandy into her mouth.

Within the next four months, three more fatalities with chloroform anaesthesia were reported, two in the U.S.A. and one in France. These deaths led to a consideration of the manner of administering chloroform and had repercussions on the design of anaesthetic apparatus.

Originally, the apparatus for the administration of chloroform was very simple, a handkerchief, a towel or even, as John Snow wrote, "a piece of lint, *a worsted glove, a nightcap* or a sponge", and such simple methods continued to be used, especially in Scotland, until quite recent times. However, many inhalers were designed in England and on the Continent as chloroform became more widely used. Of these, the most important were Charrière's, an early and effective, but somewhat cumbersome machine, and Snow's which incorporated a "wick" of blotting paper and a non-rebreathing valve.

In 1849, Snow described another apparatus which "consisted of a hydrogen balloon holding upwards of two thousand cubic inches, which was provided with a tap, and attached to a face-piece containing valves, by means of a short and wide tube. When used, a measured quantity of chloroform was put into the balloon, which was then inflated with air from a bellows; in this way the exact proportion of vapour in the air breathed by the patient was known . . . [Snow] found that 3 per cent by measure of vapour sufficed to induce insensibility in two minutes. . . . The expired air escaped by a valve, without returning into the balloon" (*Lancet*, 1849, **1**, 588). This apparatus, the first quantitative apparatus to be invented, was modified by Clover, and is generally known by his name; a somewhat similar device was used by Hewitt at the close of the 19th century for administering nitrous oxide and oxygen in known proportions.

In spite of these developments, deaths under chloroform continued to occur, and considerable alarm began to be felt, but the number of fatalities was not so very great, considering the lack of understanding of the problems of anaesthesia; world literature revealed only 393 deaths during the first 34 years of chloroform anaesthesia, and about 10 per cent of these were post-operative, the form of anaesthesia apparently having little influence on the outcome. On the

other hand, reported deaths from other anaesthetics during the same period amounted only to 48.

As a result of these continuous fatalities, there sprang up two schools of thought. The "clinical" school, headed by Sir James Y. Simpson and, after his death, by Joseph Lister, maintained that the simplest apparatus was the best and advocated administering chloroform on a handkerchief or towel. Since, they claimed, death only occurred either in light anaesthesia or from respiratory failure, the drug should be given in adequate amount and care should be taken to watch the respirations. On the other hand, the "scientific" school, led by John Snow and, after his death, Joseph Clover, maintained that death was frequently due to cessation of the heart's action, often induced by too high a concentration of chloroform in the inspired air. They advocated the use of quantitative and, therefore, less simple apparatus, and advised that a finger should be kept on the patient's pulse throughout administration.

Concern continued to be felt, and, in 1864, the Royal Medical and Chirurgical Society (now the Royal Society of Medicine) appointed a committee to enquire into the problem. The report of this committee described experiments which had been undertaken on animals, and concluded that concentration of chloroform of 2–4 per cent in air were safe, but that higher concentrations were extremely liable to lead to death from "syncope". Such an outcome was rendered less likely in the animal if the vagus nerves were divided.

The introduction of nitrous oxide and the reintroduction of ether anaesthesia, already described, led to a reduction in the use of chloroform during the last 30 or so years of the 19th century. However, chloroform still continued to be used fairly extensively, and the practice of administering atropine and/or morphine before the use of this drug seems to have begun in the 1880s.

In 1875, the British Medical Association appointed a committee, known as the Glasgow Committee, to enquire further into the problem of chloroform fatalities. The committee did not meet until 1877, and reported in 1880. The conclusion reached was that chloroform was much more injurious to the heart than ether, and a recommendation was made that ethidine dichloride should be used as a compromise, since it "stood intermediate whether as regards the time required, or the dose needed."

In 1889, the first Hyderabad "Commission", financed by the Nizam, and consisting of experiments undertaken by his resident Surgeon, Edward Lawrie, reported that, after killing 128 fully-grown dogs with chloroform, in no case did the heart become dangerously affected until after the breathing stopped. This forthright support for the "clinical" (Edinburgh) school, roused the "scientific" (London) opposition, and the *Lancet* took up the cudgels on the latter's behalf. The Nizam of Hyderabad offered a further sum of £1,000, and the *Lancet* sent (Sir) Thomas Lauder Brunton, a leading physiologist, to assist Lawrie in further experiments. This was the second Hyderabad "Commission". It reported in 1890, further reports being issued in 1891 and 1893; 588 animals had been used, and the results confirmed completely the report of the previous year, even the sceptical Brunton being convinced. The *Lancet*, however, refused to accept the situation, and the "opposition" remained unshaken in its views. In 1891, the British Medical Association elected another committee, which did not report until 10 years later. This committee requested the anaesthetists in Britain to record all their anaesthetics in 1892, and submit the records for examination; 25,920 records were considered. The report was disappointing and consisted of vague generalities, no definite conclusions being reached. In consequence, the British Medical Association appointed yet another committee in 1901; this was known as the Special Chloroform Committee. It reported in 1911; having concluded that the dosimetric administration of chloroform was the safest, and that no adverse effects upon the heart could be expected with concentrations of 2 per cent or less in air, the committee recommended the use of the Vernon Harcourt inhaler, which had first appeared in 1904.

It was also in the year 1911 that Goodman Levy "communicated a note to the Physiological Society describing a hitherto unrecognized form of sudden cardiac failure which occurred in cats under chloroform, and stating that he had, acting upon a suggestion made by Professor Cushny,

looked for and found ventricular fibrillation in such cases. At the same time he showed that an exactly similar form of death could be reproduced by injecting small doses of adrenaline into the vein of a cat lightly anaesthetized with chloroform. These observations became the starting-point of a series of experiments elucidating the conditions under which ventricular fibrillation occurs, and showing that it happens only in light chloroform anaesthesia, never in full or deep anaesthesia" (Levy, A. G. *Chloroform Anaesthesia*, 1922, London: Bale and Danielsson, p. 96). The twofold dangers of chloroform, death in either light or too profound anaesthesia, were thus explained.

As we have seen, Simpson had introduced ether anaesthesia into midwifery in January 1847. In November of that year, he turned to chloroform. The use of anaesthesia to mitigate the "curse of Eve" aroused strong objections among a class of religious folk, who, being men, could afford to be high-principled in such a matter. A Dr. Gream, for example, said that to use anaesthesia in midwifery was to "turn the lying-in chamber into a scene of drunken debauchery"; and many, both medical men and clergy, protested that this particular form of alleviation of distress was in direct opposition to the biblical authority, "In sorrow shalt thou bring forth children". Simpson, however, was equal to the occasion: he showed that the Hebrew root of the word, translated as "sorrow", really meant "struggle". Opposition to anaesthesia in midwifery was slow in subsiding. Queen Victoria herself did not dare to make use of it at the birth of Prince Arthur in 1850, although she made enquiries about it. It was not until the birth of Prince Leopold in 1853 that she allowed John Snow to administer chloroform to her; this he did intermittently, a method which then became known as "chloroform à la reine". The final seal of acceptance came when the Queen again accepted chloroform at the birth of Princess Beatrice in 1857.

Simpson was so imbued with the success of chloroform as an anaesthetic that he came to regard "chloroform" and "anaesthesia" as virtually synonymous; he would hear no argument against it, and he convinced himself that his own contribution to anaesthesia was of greater importance than the discovery of ether anaesthesia by Morton. Called upon to write an article on "Chloroform" for the *British Encyclopaedia*, he wrote it in such a way as to suggest that he was himself the discoverer of anaesthesia. This, and other public utterances, involved Simpson, at the end of his life, in an acrimonious correspondence with Henry J. Bigelow, who had been present on the historic occasion at the Massachusetts General Hospital on October 16, 1846. Simpson was not without failings; he had many enemies, chief among whom was Professor Syme; and the story of how and why he assumed his second name, "Young", indicates his forceful, tactless behaviour; yet his friends loved and respected him, and, although chloroform has lost its position as the most important anaesthetic agent, nevertheless Simpson's contributions in the field of anaesthesia alone (and there were many other fields in which he made important advances) make his memory justly renowned.

Among many others who advocated and advanced the use of chloroform is John Snow, justly regarded as the foremost anaesthetist that the world has seen. His famous book on *Chloroform and other Anaesthetics* was his last achievement, and he was seized with his fatal illness on its completion (June 9, 1858); he died seven days later. Snow, unlike Simpson, recognized that chloroform was not without its dangers, but he accepted the risk and, as he said himself, he did not allow this to stand in the way of "its ready applicability". A. E. Sansom, a close friend of Snow, issued a handbook, *Chloroform: Its Action and Administration* in 1865; this work had considerable influence and helped to retain chloroform in its place of pre-eminence. The book is interesting in that it contains an account of artificial respiration performed by electrophrenic stimulation with both surface and buried electrodes.

From the time of the beginning of the first world war, the use of chloroform ostensibly diminished. Since the reintroduction of ether anaesthesia into Britain (1872), chloroform had continued to be used on the continent of Europe, and it was by no means displaced entirely in this country. Experience with war casualties showed the advantages of nitrous oxide, and since then there has appeared an attitude of mind which

has made it seem almost reprehensible to use this agent; in some places, strictures by coroners after fatalities have influenced the profession against chloroform, an intrusion into the field of anaesthesia which is much to be deprecated. In spite of this, chloroform is still quite widely used, although the majority of its users tend to be reticent about their experiences. Dr. John Gillies found in 1948 that 97.5 per cent of Scottish general practitioners used chloroform in obstetrics, and that 80 per cent of specialist anaesthetists throughout Britain used it at least occasionally. The last important work on the subject was done by R. M. Waters and his associates. Published in 1951, *Chloroform: A Study After 100 Years*, detailed the results obtained in more than 1,100 clinical administrations, the anaesthetics being carefully monitored and recorded. They concluded that "chloroform does not deserve to be abandoned", but made certain apparently illogical reservations (see *Anaesthesia*, 1959, **14**, 130).

DRUGS RELATED TO CHLOROFORM

As we have seen the term "chloric ether" was first applied to a substance, or more probably, a mixture of unstable substances, otherwise known as Dutch Oil. Indeed, Guthrie believed that he had discovered a new method of manufacturing chloric ether, and, for some considerable time, the terms "chloric ether" and "chloroform" were used rather indiscriminately. Thus, we find that Richard Formby of Liverpool suggested the use of "chloric ether" to Simpson in 1845 (Dundee, J. W., *Anaesthesia*, 1953, **8**, 218), and it was presumably Dutch Oil which was intended.

"Chloric ether" was also used in the Middlesex Hospital as early as February 1847. Jacob Bell stated (*Pharmaceutical Journal*, 1846–7, **6**, 357) that it was "rather less powerful in its effects than sulphuric ether", suggesting that his preparation was not chloroform.

Simpson experimented with Dutch Oil (and also with acetone and nitric ether) in 1847, but found it to be insufficiently powerful. Thomas Nunneley of Leeds, however, in 1849, thought that it was a promising agent; "in a very young or feeble person, I should feel disposed to employ it in preference to chloroform", he wrote. Snow also investigated a number of compounds, including Dutch Oil, which he found to be slow in action, although he believed it to be very safe. He also experimented with ethidine dichloride (1:1-dichloroethane), a similar substance, which achieved some popularity and was eventually recommended by the Glasgow Committee of the British Medical Association. The committee also reported unfavourably on Dutch Oil, stating that it invariably caused convulsions before anaesthesia appeared. Evidently the various investigators were not using identical substances.

The 1864 Chloroform Committee advised the use of mixtures of chloroform and ether, with or without the addition of alcohol. The first move in this direction had been made by John Gabb, who, in 1848, suggested that it might "be desirable to add a little of the stimulating effect of ether to the directly sedative influence of chloroform" (*Lancet*, 1848, **1**, 521). Mixtures of chloroform and ether became popular in Southern Europe in the 1850s, the Vienna mixture, for example, consisting of one part of chloroform to six or eight parts of ether. The familiar A.C.E. mixture (alcohol, one part; chloroform, two parts; ether three parts) were invented by George Harley, in about 1860. It has the advantage over simple mixtures of chloroform and ether that the addition of alcohol made an azeotropic mixture. The 1864 Committee was unable to decide between A.C.E. and a simple mixture of chloroform, one part, and ether two parts; both retained their popularity well into the 20th century.

When, in February 1847, Flourens experimented with chloroform, he also tried ethyl chloride on animals, and found its action to be similar to that of ether. Ethyl chloride was also investigated by von Bibra and Harless during the same year, and F. Heyfelder used this agent in three patients. He thought it to be satisfactory, but stated that the volatility of the drug, its high price and difficulty of obtaining it pure, made it unsuitable for general use. In 1849, Nunneley tried ethyl bromide, and this drug obtained a measure of acceptance, being advocated by Silk as late as 1891. One of this latter agent's most famous advocates was the American surgeon, J. Marion Sims.

Meanwhile, ethyl chloride had been forgotten: the medical profession was reminded of it, however, by the description in 1890 by Redard of

Geneva of the ethyl chloride spray still in use today. Redard advocated ethyl chloride as a local refrigeration anaesthetic, and it quickly became popular; by 1891 it was being used very successfully in dental surgery in London. In the following year, Wood and Cerna of Philadelphia investigated ethyl chloride as a general anaesthetic, but came to the conclusion that the "fugaciousness" of its action would interfere with its efficiency.

However, in 1894, H. Carlson of Gothenburg, and, in the following year, Thiesing of Hildesheim both accidentally produced general anaesthesia when using ethyl chloride for dental extractions. Thiesing experimented on animals with satisfactory results. Others began to use ethyl chloride under the name "Kelene", but its acceptance depended substantially on the work of Lotheissen of Innesbruck, who used it extensively from 1896. His first death was reported in 1899, the patient being shown at autopsy to have a seriously diseased heart. The death occurred immediately after administering a further dose of ethyl chloride, and it was from this mishap, and the accounts of several others, that the idea arose that it was dangerous to administer the substance in any save "single shot" doses.

In 1901, Roland and Robinson of Bordeaux introduced "Somnoform", a mixture of ethyl chloride, 60 parts; methyl chloride, 35 parts; and ethyl bromide, 5 parts; but this mixture only achieved a short-lived reputation.

Trichloroethylene had been discovered in 1864. Its anaesthetic action appears to have been first noticed by K. B. Lehmann of Wurzburg, in 1911. He administered it to 8 cats, found induction to be unduly prolonged, and noticed the tachypnoea which is often caused by it. He also remarked on the formation of dichloroacetylene when the substance was heated in the presence of alkali (Ostlere, G., *Anaesthesia*, 1953, **8**, 21). The use of trichloroethylene as a solvent in industry led to a number of cases of poisoning, the symptoms of which frequently included prolonged or permanent palsy of the trigeminal nerve: this suggested its use in trigeminal neuralgia, for which it was first given in 1915, by Oppenheim of Berlin.

In 1934, Jackson and Herzberg, both of Cincinnati, published experiments on animals, which showed that the drug had potentialities and was apparently fairly safe. Consequently, trichlorethylene was used clinically in 304 minor operations by Striker and his associates at Cincinnati; they published an account in 1935. The drug was reintroduced in 1940 by Langton Hewer and C. F. Hadfield, at St. Bartholomew's Hospital, where it was used in the chloroform bottle of Boyle's apparatus as a supplement to nitrous oxide and oxygen anaesthesia. At first it seemed satisfactory when used in the closed circuit with soda lime, but the occurrence of several examples of poisoning with di-chloroacetylene (produced by decomposition) led to the embargo on its use with carbon dioxide absorption.

Halothane, developed by Imperial Chemical Industries, was introduced into clinical practice in a limited way in 1956. It is too soon to comment on this substance, but it has been accepted with very considerable enthusiasm, despite the fact that its properties seem to be remarkably similar to those of chloroform. Like di-vinyl ether, halothane is a "tailor-made" substance, "constructed" by chemists with the object of obtaining an anaesthetic having certain desirable qualities. Other fluorinated compounds have also been investigated and used clinically, but, so far, halothane appears to be the only one which is likely to become generally accepted.

It is to be hoped that chemists will continue their efforts to produce more anaesthetic agents which may be desirable for one or more reasons. Early investigators sought the "perfect" anaesthetic agent; the experience of the last century teaches us that this is a chimera: the "perfect" anaesthetic does not—indeed, cannot—exist, but the more agents with diverse actions which we possess, the better are we fitted to meet the demands of ever-extending surgical interventions with forms of anaesthesia which will further the requirements of the operator and decrease the risk and discomfort for the patient.

A Practice of Anaesthesia. By Dr. W. D. Wylie and Dr. H. C. Churchill-Davidson. Published by Lloyd-Luke (Medical Books) Ltd., London (1960). Pp. 1056; illustrated; tables 67. Price 105*s*.

Continuity is the advantage of the single-author textbook; multiply the authors and the reader faces new taskmasters, differing styles are introduced and the patterns of teaching change, not always for the better. Be this as it may, Wylie and Churchill-Davidson are to be congratulated upon an excellently designed treatise. They have so spread their net over the seven other authors' work as to secure a good measure of continuity. No doubt this has been possible because all the authors are St. Thomas's men.

Rightly they stress the need for anaesthetists to become familiar with the applications of the basic sciences, and this raises a fundamental question of teaching. Should these sciences be considered in a separate section, or be dealt with wherever they apply? The authors are perhaps wise in being inconsistent in tackling this problem, but they do not always appear to grasp the fundamental applications. For example, in discussing the flow of blood to various anatomical parts in the lung, they fail to stress that gaseous distribution should be considered in relation to perfusion; an alteration of this ratio could be a major cause of hypoxia.

Roughly 33 per cent of the book is devoted to the central nervous system, 31 per cent to respiration, 19 per cent to the cardiovascular system and 9 per cent deals with the metabolic and endocrine functions as they are related to anaesthesia. The reviewer cannot hope to be equally conversant with all the material in this book and may, therefore, be excused for concentrating a little on some parts more than others.

The section dealing with neuromuscular transmission and the relaxant drugs is unusually informative. Spinal anaesthesia is given a prominent place; surprisingly enough, the careful preparation of the skin of the patient's back, so vital in avoiding infection, receives scant attention. It is assumed that the skin may be sterilized without any difficulty, presumably because it is stated that infection is the one completely preventible complication. There is an appendix which deals with the care and sterilization of apparatus and instruments.

In the section dealing with respiration there is a description of lung function tests which fails to portray the combined dynamic functions which lead to the conception of reversible or non-reversible obstructive lung lesions or restrictive disease. For example, the forced expiratory volume (one second) test may be used in combination with bronchodilator drugs and the forced vital capacity to differentiate the various types of disorder.

The breath-holding test is described as a useful method for estimating cardiorespiratory reserve; what this means is not defined.

In attempting to explain how the anatomical deadspace can be estimated, there is no mention of the expiratory volume—an essential component for this measurement!

A simple indirect method for estimating arterial CO_2 tension, utilizing a rebreathing technique to measure the mixed venous CO_2 tension, from which 6 mm of Hg can be subtracted to give arterial CO_2 tension, although a major advance—which can be adapted to anaesthesia—is omitted altogether from the text. Despite the increasing use of the end-tidal sample in measuring pulmonary ventilation, the authors fail to launch a critical attack upon its value.

The appendix dealing with apparatus for artificial respiration seems an unnecessary addition as the subject is dealt with in detail in another treatise. The whole specialty of anaesthesia can no longer be conveniently confined within a single volume.

The circulatory system is well documented, but "shock" apparently still exists. The use of the term offers no help in diagnosis and indicates no specific treatment; it covers many different conditions of different aetiologies. There is nothing in the chapter on surgical shock concerning modern methods with full curarization and light anaesthesia. Neither is the point stressed that vasoconstriction, hypotension and tachycardia may be present in patients with infection (from abdominal injuries) with normal blood volumes.

The metabolic and endocrine systems are covered with unusual clarity.

Each chapter closes with a careful selection of references, and after some a bibliography has been added. There is a useful vade mecum at the end of the book, but from this are omitted tables concerning height, weight and surface area, which would have been a valuable addition. The index occupies 25 pages. The illustrations are, on the whole, excellent; a few are ill-chosen, like figure 235, which shows a box on wheels with a gauge, concertina tubing and a mask.

One admirable feature of this work is that the authors devote many words to explain the significance of the basic sciences and of pathology in relation to the work of anaesthetists. No anaesthetist can afford to be without this major work.

R. P. Harbord

The Innervation of Muscle: a Biopsy Study. By C. Coërs, Docteur en Médecine, Angrégé de l'Enseignement Supérieur, Chef du Département de Neurologie de la Clinique Médicale, Hôpital Brugmann, Brussels University, and A. L. Woolf, M.D., Consultant Pathologist, Midland Centre, for neurosurgery, Smethwick, England. Blackwell Scientific Publications (1959). Pp. 149; illustrated. Price 42*s*.

For many years the information obtained from muscle biopsies has been unsatisfactory mainly because the removed piece of muscle rarely contained neuromuscular junctions, vital structures in the diagnosis of muscle disease. The authors of this book have themselves been responsible for important advances in the field during the last few years. In 1952 Coërs introduced a method by which before removal of the muscle specimen the motor endplate region was accurately localized by electrical stimulation of the motor nerves through the skin or directly through the exposed muscle. This technique undoubtedly improved enormously the quality of the muscle specimens. Furthermore, Coërs, by combining useful techniques of nerve impregnation together with methods of staining the cholinesterase enzyme of the motor endplate, has succeeded in demonstrating structural details at the neuromuscular junction.

In this book, Drs. Coërs and Woolf present the results they have obtained by the application of these methods to the study of 450 muscle biopsies removed from patients with or without neuromuscular abnormality. In the first chapter the authors describe in detail their technique and in the second they give a very useful account of the normal histology of the neuromuscular junction region in animals and man. In the following three chapters they describe, with the help of 281 very good illustrations, the general and special pathology of the intramuscular nerves and nerve endings. All who wish to undertake similar work should consult this book because the information contained in it springs from an unrivalled personal experience. The bibliography of the book is very well covered.

However, one must add that the whole book reads like an excellent presentation of an advanced piece of research work and that the methods used, although very good, could and will undoubtedly be further improved. The other point worth mentioning is that the technique described in this present form may prove rather impractical for ordinary routine hospital work as it is quite a complex procedure which still needs the hands of a skilled team.

Eleanor Zaimis

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